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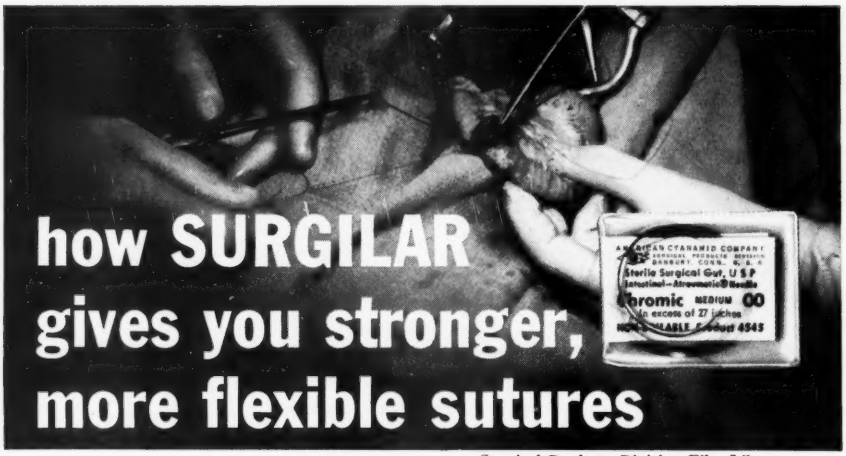

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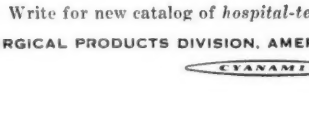

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THE ANATOMY OF THE CHOLEDOCHODUODENAL JUNCTION IN MAN

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To THE SURGEON and the internist the choledochoduodenal junction is one of the most important diminutive areas of the human body. Here is implanted an intricate musculature which causes the filling of the gallbladder, which regulates the outflow of bile and of pancreatic enzymes, and which directly or indirectly is a factor to be reckoned with in pancreatitis and the postcholecystectomy syndrome. Yet, strangely enough, some 70 years after Oddi's significant observations, the existence of a sphincter at the end of the bile duct is still being questioned.

The basic problem has been the difficulty of distinguishing, anatomically and physiologically, between the musculus proprius of the bile duct and the contiguous intestinal musculature. Yet much progress has been made. On the physiologic side the carefully designed experiments of Bergh and Layne on cholecystectomized patients have proved that the sphincter can act independently of the intestinal muscle; for spasms of the sphincter can be induced in the presence of normal rhythmic activity of the duodenum (2) and such localized spasms are accompanied by sharp pains resembling those of biliary colic (17). On the anatomic side Schwegler and Boyden (23) have shown that the musculus proprius of the common duct first appears in the human fetus some 5 weeks later than the intestinal musculature, and that it arises *de novo* from mesenchyme. It is therefore of a different order of musculature than the others both in point of time and in its looser organization. Forming first at the point where the duct penetrates the duodenum, it advances along the duct as an enveloping sheath of fibers (Fig. 20). However, early in its course it seems to induce a sprouting of fibers from the older intestinal musculature which eventually ties the bile duct to the duodenum.

It is this last feature which creates the anatomic problem. Some investigators have felt that the contributions made by the intestinal muscle are the important elements; others, like the writer and his colleagues (5, 16, 23) have maintained that the sphincters are the essential elements and that the connections with the gut musculature are auxiliary structures serving to reinforce the weak spot in the wall, to prevent the duct

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from being torn loose from the intestine by movements of the viscera and to assist the discharge of bile by erecting and shortening the papilla.

The reasons which have led the writer to re-examine the human sphincter are as follows. First, a comparison of this region in the dog (13), cat (7), chimpanzee (6), and monkey (8) has given new emphasis to the importance of the sphincter choledochus in primates. Second, in spite of evidence to the contrary, a recent paper by Schreiber has revived the old theory that the sole function of Oddi's muscle is ejaculatory—namely to pump bile into the intestine. Strongly influenced by the work of the radiologist Bernhard, Schreiber made maceration preparations of the choledochoduodenal junction, and presented drawings of the exterior of the papilla which stressed the fibers that connect the papilla with the intestinal muscle. Going beyond Bernhard, he denied the existence of any independent constrictor of the bile duct and renamed Oddi's sphincter the "M. complexus papillae duodeni." He concluded that the muscle complex always works in conjunction with (i.e., "bound to") the activity of the duodenal musculature and that it fully explains the rhythmic emptying of the bile into the intestine [if such exists in man]. Unfortunately he neglected to bisect the bile duct and dissect its inner surface. Thus he failed to see the principal fibers of the sphincter choledochus. Moreover, both he and Bernhard seem not to have been aware of important embryologic and physiologic studies having a direct bearing on this problem. Yet Schreiber's figures are so clear that a reader without firsthand experience might well conclude that such anatomic evidence must be decisive. Hence the necessity of providing corrective data.[1]

MATERIAL AND METHODS

Seven specimens of the pars descendens of the duodenum were obtained at necropsy and placed in 20 per cent nitric acid for from 26 to 40 hours. When sufficiently macerated the tunica mucosa was removed and the muscular portion of the wall was placed in 20 per cent formalin. Five of these specimens were found suitable for detailed study. After each had been hardened in formalin both sides of the choledochoduodenal junction were carefully drawn to a magnification of 10 under the binocular microscope, following which the specimens were dissected superficially. Then each was bisected lengthwise with irridectomy scissors in such a way that the plane of section passed through both the bile and pancreatic ducts or just the former. When the outline of the cut surface had been drawn, the mucous lining of the bile duct was picked out a little at a time with finely ground forceps until the muscles lining the duct were exposed. Then these were drawn. Finally, layers were pulled apart and sketches made of detailed areas. Thus, in order to understand the specimen fully, it was necessary to draw it in stages and virtually to destroy it in the process of dissection.

In 2 of the 5 specimens, bile and pancreatic ducts opened separately at the end of the papilla. In the remaining 3 the ampulla of Vater had persisted. This channel, common to both ducts, varied in length from 4 to 5.5 millimeters.

THE MUSCULATURE OF THE CHOLEDOCHODUODENAL JUNCTION

Entrance of the ducts into the duodenal wall. As described in earlier publications of fetal (23) and adult material (16), bile and pancreatic ducts enter the left surface of the pars descendens through a hiatus in the longitudinal muscle and then pass through a fenestra in the circular muscle of the gut (Figs. 2 and 7). In a representative specimen the fenestra is a transversely placed oval aperture measuring 5 by 7 millimeters (*Fen. chol.*, Fig. 7). Its superior margin lies next to the tunica mucosa, and is therefore internal (*Margo sup., s. int.*, Figs. 1 and 10). Its inferior margin lies on the surface of the pars descendens of the duodenum and s

[1]Schreiber refers to other articles in preparation, and so may have intended to pursue the matter further, but, apparently no subsequent paper has appeared.

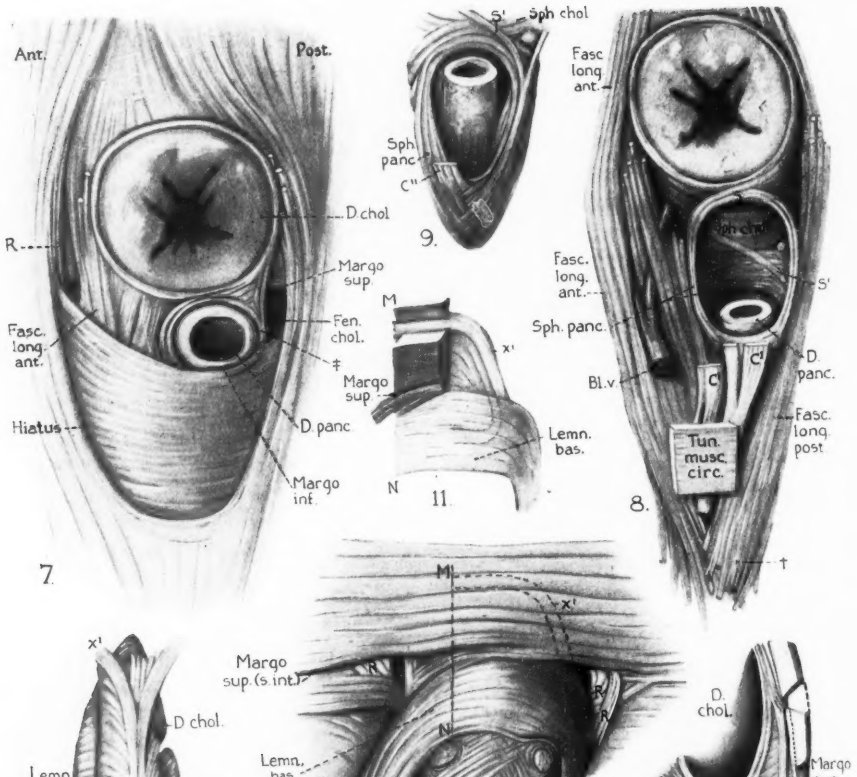
therefore external (*Margo inf., s. ext.*, Figs. 2 and 7). Both margins may be seen at the same time in sagittal sections (Figs. 5 and 17).[2]

This site of entrance of the ducts is one of several places where there is interchange of fibers between muscle layers. Such "wandering" elements may be classified as "reinforcing" and "connecting" fibers. Since they are variable, hardly any two specimens look alike (cf. Figs. 2 and 7 with Figs. 1 and 2 of the article by Kreilkamp and Boyden). Reinforcing bands, for instance, may pass from the side of the hiatus to the margins of the fenestra (viz., *R*, Figs. 2 and 7). By strengthening the corners of the aperture they prevent it from splitting further. Connecting bands may pass from the intestinal muscle to the ducts or to the papilla (viz., *A*, Fig. 2; *C′*, Figs. 8 and 13; and *X′*, Figs. 10 and 11). Occasionally a "C" band passes from the margo inferior across the fenestra (between bile and pancreatic ducts) to the opposite side of the bile duct (see asterisk, Fig. 2, and Kreilkamp and Boyden, Fig. 2). I have seen it also in the chimpanzee fetus (6). In general, one can say that it is the auxiliary apparatus (connecting and reinforcing bands) that is the most variable. The sphincters are relatively constant.

Emergence of the ducts from the fenestra. When the mucosa is removed, one exposes the base of the papilla as it emerges from under the margo superior or internus of the fenestra (Figs. 1 and 10). Just distal to the margo, and at a slightly deeper level, is a broad thin band of muscle passing across the exposed surface of the papilla. This is Schreiber's *M. sphincter basis papillae*. Because its action as a true sphincter is questionable I have renamed it "lemniscus basalis." As in the case of other auxiliary bundles, no two of these bands have quite the same connections. The one in Figure 1, for instance, has several components (there labelled *x*, *y*, and *z*). Starting below, bands *x* and *y* arise from the circular muscle of the gut (margo inf., Fig. 5). Band *x* passes into the margo superior but *y* joins *z* (which comes up from papilla) and both of these continue upward on to the opposite side of the bile duct (*y* and *z*, Fig. 1). Obviously, in this specimen, this composite band is not a true sphincter of the base although contraction of it might compress the papilla somewhat. Embryologically, this band develops as part of the musculus proprius of the duct but becomes applied to the circular muscle and receives sprouts from the margins of the window (see Plate 2, Schwegler and Boyden, 1936b). Because it is connected with the circular musculature —that is, it is composed of "connecting" fibers—Schreiber thinks that it could contract only when the gut contracts. Is it not just as logical to assume that it gets a purchase on the intestinal muscle but contracts when the musculus proprius contracts? A variation of this band may be seen in Figure 3 of the article by Kreilkamp and Boyden (16). There the band starts on the anterior side of the papilla, crosses the base superficially, then turns upward into the posterior longitudinal fascicle of the duct. A third variation is shown in Figure 10 of this paper. Here the band is more like the one pictured by Schreiber. Its fibers originate symmetrically on each side of the papilla as well as from the underlying circular muscle layer and move across the superficial surface of the base of the papilla to the opposite side of the margo superior. Its relation to the posterior longitudinal fascicle of the papilla is shown in Figures 10 to 12.

The pars inferior of the sphincter choledochus (*Sph. chol. inf.*). Before discussing the other superficial muscle layers seen in Figures 1 and 10 it is instructive to consider the strongest and most significant lamina of the musculus proprius. This is the portion exposed by splitting the papilla and picking out the mucous lining of the bile duct. Two patterns are revealed, depending on whether there is an ampulla of Vater or whether the bile

[2]The reason for adding the terms "internus" and "externus" is not only to convey additional information but also to correlate them with corresponding margins in animals like the cat and dog. In these species the originally superior margin of the embryo grows caudal to enclose the ducts in a canal of intestinal muscle. Since it is no longer a margo superior in these forms it is designated "margo internus."



and pancreatic ducts empty separately at the end of the papilla. Figures 5 and 6 are sketches of anterior and posterior halves of the first type. Lining and encircling the bile duct from the level of the fenestra to near the confluence of bile and pancreatic ducts —a distance of 6 millimeters—is a series of stout circular muscle trabeculae. These constitute the sphincter choledochus inferior. Tonic contraction of this muscle would cause reflux of bile into the gallbladder during fasting. Relaxation of the muscle in response to the hormone, cholecystokinin, would permit the bile to flow into the intestine. Doubtless secondary connections with the adjacent musculature of the gut would help expel the bile. But during fasting and in the absence of proper hormonal stimulation (as

LEGENDS FOR FIGURES 1 TO 13.

FIG. 1.[3] Major papilla seen emerging from under the circular muscle layer of the gut after removal of the tunica mucosa. Note: the internal margin of the choledochal window (*Margo sup., s. int.*); the thin flat band passing across the base of the papilla (*Lemn. bas.*); the sphincter ampullae at the apex of the papilla; and numerous glands (*Gl.*) penetrating the meshes of the many layered musculus proprius ensheathing the papilla.

FIG. 2. Undissected lesser curvature of the pars descendens of the duodenum at the point of entrance of bile and pancreatic ducts. Note *hiatus* in longitudinal muscle layer and the oval window (*Fen. chol.*) in the circular muscle layer of the gut. In this specimen the margo inferior (s. ext.) is interrupted by a bundle of circular muscle fibers (*) which crosses the fenestra between the two ducts. (For more usual pattern, see Fig. 7). *A*, Broad band connecting side of bile duct with margo inferior; *R*, band reinforcing angle of window by connecting longitudinal and circular layers of gut (cf. *R*, Fig. 7).

FIG. 3. Deeper level after partially removing muscle layers of gut. The observer is now looking at the left posterior wall of the major papilla, i.e., at the normally hidden surface next to the gut wall. *A*, The band shown in Figure 2 (For its insertion into margo inferior, see *A*, Fig. 5); *B*, fibers passing into anterior longitudinal fascicle; *C*, fibers crossing deep surface of papilla; *S*, S-shaped fibers underlying the band labelled with an asterisk in Figure 2.

FIG. 4. A still deeper layer of muscles at the base of the papilla, exposed by removing some fibers and by swinging the wall of the fenestra and the base of the papilla away from each other. This reveals the network of fibers covering the base of the papilla, and its partial origin from the curved sheet of muscle labelled *x'*. This sheet is applied to the circular muscle of the gut above the margo superior, but it can be peeled off as a discrete layer. This indicates that while it receives fibers from the opposite side of the margo, much of it is musculus proprius encircling the base of the papilla. (For embryonic development of this portion of the sphincter choledochus superior, see Schwegler and Boyden, 1937b.)

FIG. 5. Sagittal section of bile duct exposing cavity of anterior half of the bisected papilla. The pancreatic duct is just deep to the plane of section, but 3 arrows indicate its pathway. The mucous lining has been retained only in the region of the ampulla (*Tun. muc.*). That of the bile duct has been removed to show the muscle trabeculae lining the bile duct and forming the principal component of the sphincter choledochus inferior. Note that the sphincter ends abruptly at the beginning of the ampulla. At the upper end note the 3 layers that contribute to the musculature around the bile duct. Layer 1 is in the same plane as that labelled *x* and *x'* in Figs. 1 and 4. Layer 2 is in the same plane as that labelled *Sph. chol. sup.* in Figure 4 (see discussion in text). Layer 3 is next to the mucous membrane and forms the major component of the sphincter choledochus inferior. However, all 3 layers anastomose in places and so form an interweaving network of fibers around the bile duct (cf. Figs. 19 and 21). The thick septum separating bile and pancreatic ducts consists chiefly of sphincter fibers enclosing the bile duct.

[3]All drawings are the work of Jessie W. Phillips.

A few pass around the pancreatic duct to the outside of the papilla. *A*, *x*, *y*, insertion into the margo inferior of bands labelled *x* and *y* (in Fig. 1) and *A* (in Figs. 2 to 4).

FIG. 6. Portion of posterior half of bisected bile duct. This shows the continuity of the superior and inferior portions of the sphincter choledochus.

FIG. 7. Undissected lesser curvature of pars descendens of duodenum (cf. Fig. 2). Note *hiatus* in longitudinal muscle layer and oval window (*Fen. chol.*) in circular muscle layer of gut. Obviously this specimen differs from that shown in Figure 2 by the greater abundance of fibers that constitute the anterior longitudinal bundle (cf. *Fasc. long. ant.*, Fig. 12). The double dagger represents a portion of the posterior longitudinal bundle (cf. ‡ in Fig. 13). *R*, Fibers reinforcing the fenestra.

FIG. 8. Deeper level after removal of the tunica muscularis of the gut. The upper segment of the pancreatic duct has also been removed to expose the sphincter fibers lying in the septum between the two ducts. *S*, *S'*, S-shaped fibers encircling both ducts; *C'*, connecting fibers that pass from the deep side of the circular muscle layer of the gut to the wall of the pancreatic duct. The dagger in Figures 8 and 10 indicates those fibers of the two longitudinal bundles which spray out onto the mucosa.

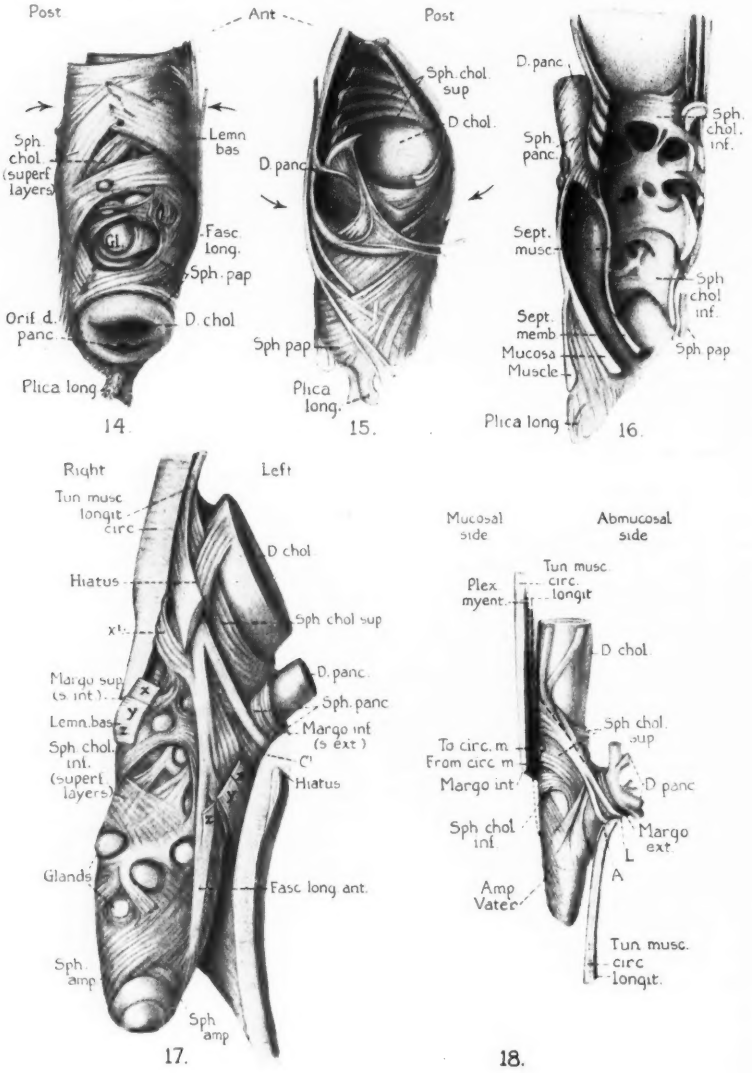
FIG. 9. Sphincter pancreaticus exposed by removal of the overlying longitudinal fascicles shown in Figure 8. (*S'*, represents the same S-shaped bundle in the two drawings.) Beginning above, between bile and pancreatic ducts, fibers of the pancreatic sphincter pass obliquely downward on either side of the pancreatic duct to interdigitate on the deep side of the papilla. *C''*, connecting fibers which pass upward to join the anterior longitudinal fascicle.

FIG. 10. Superficial surface of major papilla emerging from under the margo superior (cf. Fig. 1). In this specimen the tip of the papilla had been sliced off before receipt of specimen. The most striking feature is the thin but unusually broad basal band (*Lemn. bas.*). This seems to be a continuation of the margo superior, but actually it lies at a slightly deeper level, i.e., in the first of the three planes of the musculus proprius noted in Figure 5. For, if the side of the margo superior to the viewer's right be cut away (as illustrated in Fig. 11) the basal band will be seen to extend upward under the margo and to be applied to the deep side of the circular muscle above the margo superior. Distally, the basal band swings around the papilla on each side to terminate in three ways: to join the anterior and posterior longitudinal bundles (*Fasc. long. ant.* and *post.*, Figs. 12 and 13); to insert on the circular muscle underlying the papilla (*y*,); and to fan out onto the contiguous tunica mucosa (†). *R*, fibers reinforcing angles of fenestra.

FIG. 11. Detail showing relation of lemniscus basalis to margo superior. (The line *MN* corresponds in position to the line similarly lettered in Fig. 10.)

FIG. 12. Anterior side of papilla showing anterior longitudinal bundle (*Fasc. long. ant.*). Note extensive spread of fibers onto bile duct (cf. Figs. 7 and 8).

FIG. 13. Posterior side of papilla showing connections of posterior longitudinal bundle (*Fasc. long. post.*). The double dagger represents the bundle similarly designated in Figure 7.



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after a carbohydrate meal) even peristalsis of the gut will not relax the sphincter.

Figure 16 displays the bisected papilla of the second type. Again stout circular trabeculae line the bile duct for a distance of 6 millimeters. These also begin at the level of the fenestra but thin out and end 2 millimeters from the orifice. The holes between trabeculae permit the passage of glands. The sphincter choledochus may also be seen in cross section as the innermost circular layers of muscle around the duct (*Sph.*, Figs. 19 and 21). Outside of this are 1 to 3 thinner layers which encircle the outer bulging portions of the glands or form obliquely crossing strands (*Sph.'*). These in-

FIG. 14. Superficial surface of a papilla having separate orifices for bile and pancreatic ducts. Arrows, margo superior (s. int.) (cf. Fig. 1). Note various layers of sphincter choledochus and a terminal sphincter papillae which corresponds, in position, to sphincter ampullae of Figure 1.

FIG. 15. Reverse side of same papilla (cf. Figs. 8 and 9). Arrows, site of margo inferior (s. ext.) (cf. Fig. 7).

FIG. 16. Longitudinal section through both ducts. Trabeculae of sphincter choledochus inferior line bile duct for 6.5 millimeters. These end 2 millimeters from orifice. See Figure 5 for a corresponding view of papilla with an ampulla of Vater.

FIG. 17. Assembly drawing of the human choledochoduodenal junction and major papilla as seen from the anterior side with the tunica mucosa removed. This is a composite drawing designed to illustrate the auxiliary musculature, i.e., the strands passing from the tunica muscularis to the musculus proprius of the ducts and papilla. The anterior longitudinal fascicle has been narrowed somewhat, in order to display relations of underlying layers. Obviously the strongest layer of the sphincter choledochus inferior cannot be seen in this view since it lines the bile duct. Therefore this figure must be supplemented by Figure 5. Before identifying the auxiliary muscles find the hiatus in the longitudinal muscle—here interrupted to show underlying structures—and the two margins of the oval fenestra through which the ducts enter the intestinal wall. Then note: the lemniscus basalis (with components *x*, *y*, and *z*); connecting bands such as *C'*, *x*, and *x'*, passing from the tunica muscularis to the ducts or papilla; and that portion of the sphincter choledochus superior which arises above, in the plane of the longitudinal muscle of the gut. In the main, the auxiliary bands seem to be acting upon the long axis of papilla or affording anchorage for outermost constricting bands.

FIG. 18. A comparable view of the choledochoduodenal junction of the rhesus monkey, reconstructed from specimens that are being prepared for publication in the *Anatomical Record*. In this species the superior portion of the sphincter choledochus is better developed than the inferior portion. It is surrounded by bands having connection with both longitudinal and circular muscle layers of the duodenum. For instance, a V-shaped band *A* originates from the circular layer of the margo externus and extends upward to the mucosal side of the bile duct. Then, without circling the duct, it descends to the opposite side of the margo externus. Some of the fibers continue upward on the bile duct. It is like a sling holding down the extramural part of the duct. At the pancreatic end it is joined by band *L* which forms a sling around the pancreatic duct—there blending with the sphincter pancreaticus and the longitudinal muscle of the gut. The specific sphincter fibers of the sphincter choledochus superior lie deep to these bands and encircle the bile duct. In addition to the connections with the duodenal muscle described, other fibers on the deep side of the margo internus cross to the opposite side of the bile duct thus resembling certain attachments of the human papilla. As the bile duct descends into the fenestra the sphincter fibers become more delicate. This is the sphincter choledochus inferior of the monkey. In man this is the most strongly developed portion. Some 2 millimeters below margo internus the two ducts unite to form the ampulla of Vater. Its musculature is thin and of obliquely longitudinal fibers. Outside of these lie scattered circular strands.

clude the peripheral layers which Schreiber sketched and which he believed were concerned merely with emptying the glands and with exerting tension on the mucosa. In the writer's specimens these outer fibers often connect with the innermost layer and so supplement the action of the deeper sphincter in wringing out the contents of the duct.

The pars superior of the sphincter choledochus (*sphincter choledochus superior*). This is the funnel-shaped extramural portion of the muscular sheath which surrounds the bile duct just before the latter enters the wall of the duodenum. In the fetus (23, II) the first portion of the sheath to differentiate from mesenchyme is that part within the fenestra. Then differentiation proceeds in both directions—extramurally as well as intramurally. Thus the superior portion of the sphincter choledochus is continuous with the inferior portion yet differs in position and composition. Doubilet mentions that he cannot see this portion in the living, but since his sphincterotomies stop short of the fenestra, one would not anticipate that he would encounter this portion. It does not extend more than 5 or 6 millimeters above the margo inferior. Nuboer has pictured this portion of the sphincter in his excellent transverse sections of the junction. It is visible in sections of the fetus, it is strikingly developed in the monkey (Fig. 18), and attention is now called to this segment in Figures 2 to 6.

This segment of the musculus proprius is the hardest to depict and to describe because of its composite structure. Starting with the exterior of the duct (Fig. 2) one sees a series of muscular arches swinging down around the bile duct and forming collectively a funnel. (Incidentally, these would offer increasing resistance to the passage of a calculus.) Such arching bundles seem to originate in the plane of, and to be connected with, the longitudinal muscle of the gut. While many of these encircle the duct contiguous ones pass to the margo inferior (*A*, Figs. 2 and 3); others join the fasciculus longitudinalis on the sides of the

papilla (viz., *B*, Fig. 3), or swing obliquely around the papilla (*C*, Fig. 3). A lower set of arches (labelled *x'*, Fig. 4) arises chiefly from the inner side of the margo superior and passes into the base of the papilla. As indicated before, all the fibers of this complex do not arch around the bile duct, but those that do give rise to the sphincter choledochus superior. Its outer fibers (*Sph.'*, Fig. 19) get their purchase from the contiguous layers of the gut, and its inner layer (*Sph.*) is continuous with that of the sphincter choledochus inferior (*Sph.*, Figs. 19, 21, and 5).

The terminal musculature of the papilla. In the fetus there is always an ampulla of Vater, but as development proceeds the ampulla frequently undergoes involution (23, I). Nevertheless, the muscle which sheaths the fetal ampulla remains in all cases. If the ampulla persists it becomes the sphincter ampullae (Fig. 1). If the ducts open separately (Fig. 14) it becomes the sphincter papillae (Schreiber's sphincter pori papillaris).[4]

A sphincter ampullae is shown in Figures 1 and 5. It is formed in part by fibers that swing around from the anterior side of the papilla and in part by fibers that encircle the orifice. On the dorsal side of the apex there can be a crossing of fibers from anterior and posterior sides (Fig. 3). Doubilet mentions that when the papilla is stroked in the living, the contraction starts around the orifice and moves upward.

A sphincter papillae is shown in Figures 14 and 16. In this specimen the papilla has been detached from the intestinal wall. Superficially the terminal sphincter is much like that shown in Figures 1 and 5, except that it encloses both ducts instead of a passage common to both.

A further point of interest is the muscular septum that separates bile and pancreatic ducts. In the type having an ampulla of Vater (Figs. 5 and 21) the septum is thick and is composed chiefly of trabeculae of the sphincter choledochus inferior. It ends abruptly at the junction of the two ducts. In the type in which the ducts empty separately, the septum continues to the orifice as a thin membrane but the sphincter portion fades out about 2 millimeters from the end (*Sept. musc.*, Fig. 16).

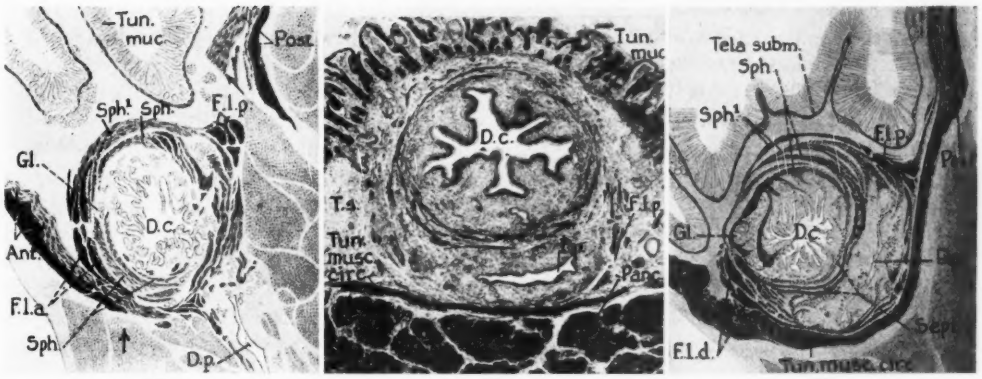
In a recent article Doubilet presents a diagram designed to show that just before the bile duct joins the pancreatic duct it expands into a dilated chamber which facilitates entrance of the duct from below with an instrument. However, this is the segment having the thickest sphincter fibers, so that one wonders whether this appearance may not have been due to relaxation of the muscle during anesthesia.[5]

The musculature of the ductus pancreaticus. Thus far 2 sphincteric bands have been mentioned by means of which the pancreatic duct could be compressed at the same time as the bile duct: (1) the "figure 8" or S-shaped fibers that encircle both ducts at their point of entrance into the gut wall (*S*, Figs. 3 and 8)—and sometimes lower down (*S'*, Fig. 8)—and (2) the common sphincter of both ducts at the end of the papilla (Figs. 5 and 14). In addition to these, some of the fibers that lie between bile and pancreatic ducts swing obliquely around both sides of the pancreatic duct to decussate on the deep side of the papilla (Figs. 3, 9, and 15). In general, there is much less muscle around the pancreatic duct than the bile duct.

Aside from these constrictive bands there are longitudinal fibers that pass from the duct upward to the margo inferior (Fig. 3) and other bands that pass from circular muscle of the gut up to the duct (*C'*, Figs. 8 and 13).

[4]Such a common terminal sphincter around the separately opening ducts is the usual arrangement in the dog (13). To emphasize its homology with the sphincter ampullae, even though the ampulla no longer persists, the writer named it the "sphincter ampullae"; but preferably also, in the dog, it should be called sphincter papillae.

[5]Incidentally, Doubilet labels this dilated preampullar portion of the bile duct "Ampulla of Vater"—a most confusing designation. Abraham Vater (4) described the segment that now bears his name as "the place of the mingling of the bile with the pancreatic juice" (i.e. the confluence of the ducts). When he bound the orifice of the papilla and then injected wax into the bile duct in the direction of the intestine "the waxy material not only penetrated into the excretory canal of the pancreas, but around the opening [of the bile duct] there was raised at the same a tubercle going around that [orifice] in a circular manner nevertheless uneven and tortuous, which we have for the diverticulum of the bile and the place of its mingling with the pancreatic juice."



19. 20. 21.

FIGS. 19 and 21. Transverse sections through the choledochoduodenal junction of a 39 year old man (Taken from Figs. 15 and 16 of the article by J. F. Nuboer, *Frankf. Zschr. Path.*, 1931, 41: 198-249.) The following legends have been added to facilitate comparison of sections and dissections.

FIG. 19. Section through the choledochal fenestra showing entrance of bile and pancreatic ducts (*D.c.* and *D.p.*) into the duodenum. Arrows indicate margins of window; *Ant.*, *Post.*, anterior and posterior walls of tunica muscularis; *F.l.a.*, *F.l.p.*, anterior and posterior longitudinal fascicles; *Sph'.*, *Sph.*, outer and inner layers of sphincter choledochus in region of transition between its pars superior and pars inferior; *Gl.*, glands passing between trabeculae of sphincter to reach surface of papilla.

FIG. 20. Transverse section of major papilla in a 34 week old fetus (43 cm.) (Taken from Fig. 5 of the article by E. A. Boyden in *Surgery*, 1937, 1: 32 and from work of Schwegler and Boyden). This section is taken at the same level as Figure 21 and indicates fetal appearance of sphincter choledochus inferior (*Sph.*).

FIG. 21. Transverse section through middle of papilla, in tela submucosa, showing septum between bile and pancreatic ducts (cf. Fig. 5). Note that the septum (*Sept.*) is composed chiefly of the inner layers of the sphincter choledochus inferior.

The fasciculi longitudinales. These are 2 longitudinal bundles of muscle applied to the anterior and posterior sides of the major papilla. They are best shown in anterior and posterior views of the papilla (Figs. 12 and 13). They vary in size and composition from specimen to specimen. From above they receive fibers from the deep side of the margo superior (Figs. 1 and 10), from the longitudinal muscle bordering upon the hiatus (Fig. 7) and from the sides of the ducts (Figs. 12 and 13). Below they pass to the underlying circular layer of the gut (cf. Fig. 3B, Kreilkamp and Boyden) or connect with the superficial network surrounding the papilla (Fig. 1) or finally spray out onto the adjacent tunica mucosa (dagger, Fig. 10). All in all these two bundles would seem to serve the dual purpose of an axial skeleton and a common pathway by which extrinsic or intrinsic muscles may gain attachment to the papilla or exert traction upon it.

The sphincter choledochus of the monkey—a preliminary report. In Figure 17 an assembly drawing of the human choledochoduodenal junction is presented as a means of summarizing the external relations of the major papilla (see description of figure). Beside it has been placed a comparable assembly drawing of the corresponding junction in the rhesus monkey (Fig. 18). This sketch is a reconstruction of dissections being prepared for publication in the *Anatomical Record* (8). It records the fact that the bile duct does not pass through a funnel in the intestinal musculature as it does in the cat and dog. Also it shows that the superior (extramural) portion of the sphincter choledochus is better developed in the monkey than in man. One may speculate that this is due to the greater stresses and strains to which the bile duct is subjected by the arboreal life of the macaque. By contrast, the inferior (intramural) portion of the bile duct is much less well developed in the monkey although in man it constitutes the strongest component of the sphincter choledochus. Furthermore, the terminal musculature of the papilla is so

delicate in the monkey that one questions whether contraction of it would cause reflux of the bile into the pancreatic duct. In any event it is not without significance that the choledochoduodenal junctions in primates such as man, the chimpanzee, and the monkey so closely resemble each other in fundamental pattern.

DISCUSSION AND CONCLUSIONS

Space does not permit detailed discussion of Schreiber's M. complexus papillae duodeni. A full account of it may be found in Michels' book. Suffice to say that the thin band-like part which he called the sphincter basis papillae (cf. *Lemn. bas.*, Figs. 1 and 10) is considered by him to be the principal sphincter and to be a part of the circular muscle of the gut which, of necessity, contracts with the gut. The writer (16), in an earlier study of similar macerated preparations, has pointed out that this is a minor portion of the "sphincter of Oddi" which arises embryologically from mesenchyme as part of the developing musculus proprius of the bile duct and which receives sprouts from the adjacent margo superior.

The portion which Schreiber calls the "M. dilatator papillae" is not a discrete layer, but consists merely of obliquely longitudinal fibers in the superficial muscular network of the papilla. Instead of an outer circular and inner longitudinal layer, there is a lattice-like structure in which fibers surround the superficial portion of the glands and run in many directions.

It would appear, therefore, that a display of merely the surface musculature of the major papilla is inadequate. For surface views (Fig. 17) show chiefly those auxiliary fibers which reinforce the margins of the fenestra or connect it to the papilla, and such other surface fibers as ensheath the papilla. The deeper sphincter musculature, which Schreiber failed to find, is revealed only when the bile duct is split and the lining mucosa removed (Figs. 5 and 16).

When this is done it becomes evident that the musculature of the major papilla is not a mechanism whose only competence is pumping bile into the intestine in compulsory co-ordination with peristalsis. On the contrary, the presence of a substantial layer of circular fibers ensheathing the intramural portion of the bile duct confirms Oddi's original discovery of a sphincter choledochus. The crucial experiments of Bergh and Layne (1, 2, 17) upon cholecystectomized patients show that this muscle regulates the flow of bile into the duodenum. During fasting there is sustained resistance to the flow of bile even though the duodenum may be undergoing rhythmic contractions. After ingestion of magnesium sulfate or egg yolk, the resistance of the sphincter drops slowly from a level of 14 cubic centimeters of water to 11 or 7 cubic centimeters, respectively, during an average period of 17 minutes. Then it returns slowly to the 14 cubic centimeter level. After a carbohydrate meal the resistance is not lowered even though peristalsis is active. The inference from these and other studies is that the hormone cholecystokinin acts simultaneously upon both gallbladder and sphincter choledochus, contracting the one and relaxing the other (9).

An important issue that remains to be solved is whether the sphincter can be made spastic through psychosomatic stimulation. Indirect evidence—such as that supplied by human vagotomies (15) and the negative effect of faradic stimulation of the gut upon the rate of emptying of the human gallbladder (10)—suggests that in this respect man differs from animals like the cat (7). If this be true, then the postcholecystectomy syndrome must be explained on such grounds as an irritable sphincter, the spastic contraction of which is caused by local inflammation, or by the presence of stones or by the pathology of associated organs. Such causes are outlined by Cole, Ivy, Walters, and others in recent discussions of this syndrome. Direct evidence, however, might still be obtained if surgeons with access to cholecystectomized patients would employ the carefully controlled experimental methods by which Bergh and

Layne demonstrated the physiologic independence of the human sphincter and its prompt response to sudden increase of pressure in the biliary duct system.

Finally there remains the question of the participation of the papillary musculature in the expulsion of bile. Bernhard concluded that the sphincter of Oddi is not only a closing muscle but that rhythmic expulsion of bile from the common duct into the duodenum is mediated by the independent ejaculatory activity of the papillary musculature. These conclusions were based on his study of barium cholangiograms in cholecystectomized patients with choledochoduodenostomies. As soon as the barium paste passed from the stomach into the duodenum he observed that the sphincter became active as a propulsive organ. Momentary constriction took place so fast that it could only be captured by accident. He attributed this activity of the sphincter to the stretching of the duodenum and the onset of peristalsis. Yet he failed to explain Bergh's observation that after a carbohydrate meal the pressure within the bile duct of cholecystectomized patients is not lowered; that is, the sphincter permits no measurable flow of bile notwithstanding continued and active peristalsis.

Very recently the physiologist Ritter has paved the way for reconciling these contradictions by showing that two kinds of behavior can be observed in the papilla of living animals. Employing urethane anesthesia, microfilms, and binocular lenses he was able to take moving pictures of the papillae of frogs and rabbits through an incision in the duodenum. Following a short period of relaxation of the sphincter he observed a contraction ring pushing forward from the base of the papilla to its apex. Thereupon the papilla erected itself steeply and remained a moment in that position. Then through sudden relaxation the mouth of the papilla opened. Meanwhile as a new constriction of the base paved the way, bile was expelled into the intestine. This manner of discharge seemed to exemplify the principle of a suction pump. However, when magnesium sulfate was dropped into the duodenum, a few superficial contractions of the papilla were succeeded by sudden relaxation. There followed mass expulsion of bile through a wide open sphincter under the contractile force of the gallbladder. Ritter concludes that in these animals there is a pumping mechanism at the papilla, but that its force is small and that its importance should not be exaggerated at the expense of the more forceful expulsion of bile exerted by the gallbladder.

CONCLUSIONS

As the bile and pancreatic ducts enter the duodenal wall they become invested by a many layered sheath which consists primarily of a musculus proprius of sphincteric character. This is anchored to the choledochoduodenal junction by auxiliary fibers derived from or attached to the intestinal musculature.

Functionally the most important element is the sphincter choledochus which lines the submucosal segment of the bile duct for a distance of more than 5 millimeters. Tonic contraction of this muscle is responsible for the filling of the gallbladder in the intervals between meals. Its relaxation under appropriate stimuli permits the discharge of bile into the intestine.

Surrounding the end of the papilla is a terminal musculature consisting of a sphincter ampullae or of a sphincter papillae depending upon whether the ducts open into the ampulla of Vater or separately. Contraction of the former may result in reflux of bile into the pancreatic duct; contraction of the latter would impede the outflow of juices in both ducts.

The auxiliary fibers, acting in conjunction with the musculus proprius may erect the papilla and assist in the discharge of bile, but contraction and relaxation of the sphincters are the activities of major importance.

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THE PRODUCTION AND CLOSURE OF EXPERIMENTAL CARDIOAORTIC FISTULAS

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CONGENITAL ANEURYSM of the aortic sinus of Valsalva is an uncommon and usually asymptomatic lesion. However, rupture of such an aneurysm ordinarily results in a fistulous communication between the base of the aorta and the right side of the heart. The clinical course of patients with such fistulas is one of rapidly progressive cardiac failure and death. The need for prompt and adequate surgical repair of such lesions is apparent. This report describes an experimental method for the closure of fistulas between the sinuses of Valsalva and the right side of the heart.

METHOD

Plastic sponge prostheses shaped like golf tees were made from compressed polyvinyl (ivalon) sponge. A block of sponge measuring 7 by 10 by 2½ centimeters was washed and compressed by stainless steel blocks and C clamps into the shape of a T. The sponge was compressed to approximately one-sixth of its original thickness. With the blocks in place, it was autoclaved for 15 minutes and baked an additional 15 minutes in a dry sterilizing oven (160 degrees C.). The resulting T shaped block was then cut into slices of appropriate size, and the prosthesis fashioned into the shape shown in Figure 2. The diameter of the flattened head was 4 to 5 millimeters and that of the shaft 2 to 3 millimeters. Immediately prior to use, it was sterilized by boiling.

Dogs, weighing 15 to 20 kilograms, were anesthetized with intravenous pentothal and cooled by immersion to a final rectal temperature of 33 degrees C. The right side of the chest was entered through the fourth intercostal space and traction ligatures placed around the superior and inferior venae cavae. The azygos vein was ligated, and the pericardium opened anterior to the phrenic nerve. The right atrial appendage was retracted inferiorly to expose the root of the aorta. The adventitia of the aorta was excised and retracted to each side by means of silk sutures. Stay sutures were then placed in the body of the right atrium. Incisions were made in the aorta and right atrium following the application of partially occluding clamps (Fig. 1).

In 10 animals a fistula was created between the noncoronary aortic sinus and the right atrium. After occlusion of the venae cavae, the clamps were removed from the atrium and aorta. The right index finger was placed in the atrium just superior and medial to the opening of the coronary sinus. A modified Reverdin needle was then introduced through the aortic incision and advanced into the noncoronary sinus until its tip was palpated by the finger within the right atrium. A tract was created by advancing the needle through the aortic wall and out into the atrium (Fig. 2). A heavy ligature was threaded into the eye of the needle and the needle withdrawn from the aorta. The ligature then passed from the aorta through the newly created tract and into the atrium. The shaft of the prosthesis was tied to this ligature, and the prosthesis was pulled into the aorta so that its proximal flattened end lay behind the aortic leaflet. The shaft occluded the tract and was brought out through the atrial incision. The partially

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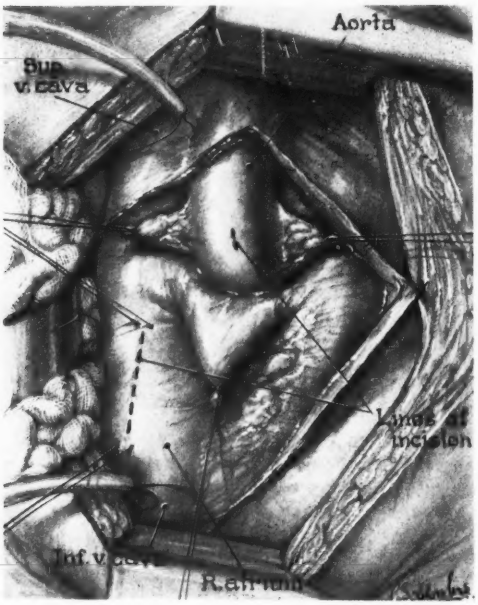


FIG. 1. Operative exposure prior to inflow occlusion. The sites of aortic and atrial incisions are indicated.

occluding clamps were then reapplied to the aortic and atrial incisions and circulation re-established. These incisions were closed with continuous over-and-over sutures, the tail of the prosthesis being incorporated into the atrial suture line (Fig. 3).

In 11 dogs a tract was created between the right coronary sinus and the right ventricle. In these dogs the approach was also through the right atrium but the index finger was placed in the ventricle beneath the septal leaflet of the tricuspid valve. The Reverdin needle was introduced into the right coronary sinus and was advanced into the right ventricle and then into the right atrium at a point just medial to the septal leaflet. The prosthesis was introduced so that its head lay behind the right coronary leaflet and its shaft passed from the ventricle across the tricuspid valve. The tail of the prosthesis was again incorporated into the atrial suture line (Fig. 4).

Aortic and left ventricular pressures were measured 1 week postoperatively. A No. 6 Cournand catheter was introduced through the femoral artery and advanced into the left ventricle. Pressures were recorded by means of a Statham P-23-A transducer and a direct writing recorder. Following catheterization, the animals were sacrificed at 1 to 4 week intervals.

RESULTS

It was initially considered that the prosthesis might interfere with aortic valve function and produce either aortic stenosis or insufficiency. The left ventricular catheterizations revealed that no animal had a systolic gradient across the aortic valve. In all, the central aortic pulse pressure tracings were normal, indicating the absence of any significant aortic insufficiency (Fig. 5). At autopsy, the aortic valve leaflets were undamaged confirming the catheterization studies. The aortic and atrial portions of the prostheses were covered with glistening pseudoendothelium. In no instance was there encroachment upon the orifice of a coronary artery. The fistulous tracts were found to be completely obliterated by the shafts of the prostheses which were infiltrated with dense connective tissue. There were 2 operative deaths among the 21 animals; one from anesthetic overdosage and the other from hemorrhage.

DISCUSSION

In 1949, Jones and Langley collected 20 cases of ruptured congenital sinus of Valsalva aneurysms from the literature and added 1 case of their own. Since that time, 15 further instances of this anomaly have been described. Two additional patients with this lesion have recently been studied at the National Heart Institute.

Congenital aneurysms of the aortic sinuses of Valsalva characteristically involve the right coronary sinus and noncoronary sinus only. In those instances reported thus far, aneurysms of the noncoronary sinus have always ruptured into the right atrium while rupture from the right coronary sinus has led to fistulas into the right ventricle, right

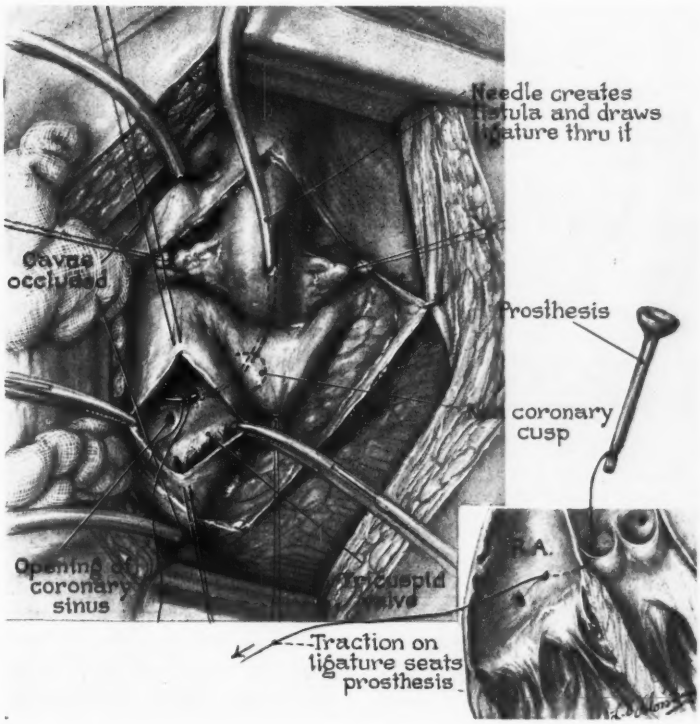
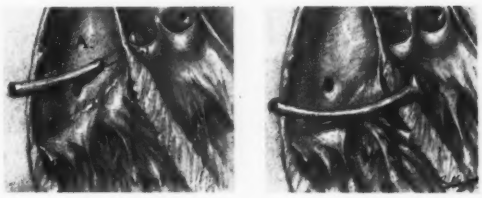


FIG. 2.

FIG. 3.



a b

FIG. 4.

FIG. 2. The fistula is created between the aorta and right atrium with a modified Reverdin needle. A heavy ligature is drawn through it, and the prosthesis is introduced through the aortic incision.

FIG. 3. The aortic and atrial incisions are closed; the tail of the prosthesis is incorporated into the atrial suture line.

FIG. 4. Final position of the prosthesis in fistulas created between (a) the noncoronary sinus and right atrium and (b) right coronary sinus and right ventricle.

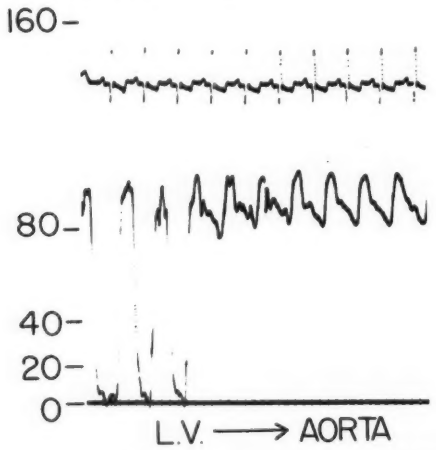


FIG. 5. Pull-out tracing across the aortic valve, illustrating the absence of a systolic gradient and a normal central aortic pulse tracing.

atrium, or pulmonary artery. Edwards has pointed out that the essential pathologic lesion is a lack of continuity between the aortic media and the annulus of the aortic valve.

Lillehei (3) and Bahnson have recently closed such cardioaortic fistulas by suture from the right side during total cardiac bypass. In the method described, the continuity of the aortic media would be restored, as suggested by Edwards, by bridging the defect with a prosthesis introduced from the aortic side. It is realized that the acute fistula created in these experiments does not duplicate the pathologic anatomy of the clinical lesion. However, these experiments have shown the feasibility of introducing a prosthesis into the aorta during a brief period of inflow occlusion without the hazards of extracorporeal circulation.

This operation has recently been successfully performed in a 28 year old man in whom an aneurysm of the right coronary sinus had ruptured into the right atrium. When follow-up studies have been completed, this case will be reported in detail.

SUMMARY

An experimental method for the closure of cardioaortic fistulas is described. Acute fistulas were created in a group of 21 dogs and subsequently closed by means of a plastic prosthesis introduced through the aorta during a brief period of inflow occlusion. Postoperatively, left heart catheterization revealed no evidence of aortic stenosis or insufficiency. At autopsy, the fistulous tract was completely obliterated by the prosthesis which was densely infiltrated with connective tissue.

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THE EXPERIMENTAL USE OF PLIABLE PLASTIC TUBES IN THE RE-ESTABLISHMENT OF GASTROINTESTINAL CONTINUITY

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DURING RECENT YEARS the Billroth I type of partial gastrectomy has enjoyed a revival of interest and of use. After the execution of a satisfactory gastric resection in the presence of a diseased, scarred duodenum, the problem of gastroduodenal anastomosis without undue tension can, on occasions, be a difficult one. The successful experimental interposition of segments of jejunum and transverse colon between the stomach and duodenum has been reported by Henley and Moroney. This procedure, of course, necessitates meticulous attention to preservation of blood supply and an additional anastomosis.

It is well established that nylon tubes serve as relatively satisfactory substitutes for the aorta, as reported by Shumacker and associates and by Barnett. This porous material allows ingrowth of granulation tissue through the wall so that nourishment of the endothelial lining, which has grown in from the adjoining vessel, is assured. Although it is generally accepted that solid tubes do not serve as satisfactory gastrointestinal substitutes, it was thought that a porous material might be invaded by granulation tissue so as to support an ingrowth of epithelium. Initial leakage through the cloth would be prevented by wrapping it with omentum. This structure would also serve to initiate the invasion by granulation tissue. Our concern relative to the fate of nylon tubes implanted between the stomach and duodenum led to the following experiments.

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MATERIALS AND METHODS

The cloth tubes used for the re-establishment of gastroduodenal continuity were constructed from nylon filter fabric which has a wrap thread count of 232 strands per inch and a filler thread count of 96 strands per inch. A pattern of the desired dimension was traced onto the surface of the cloth. There is, of course, no intraluminal gastroduodenal pressure comparable to the aorta, and for this reason measures were taken to prevent collapse of the tube. At a point 1 centimeter from the end of each tube, a seam was taken around the circumference, through which a strand of wire was introduced. A 5 millimeter cuff was next folded back on each end and sewed, thus giving a smooth, nonfrayed edge for anastomosis. Construction of the tube was completed by placing a seam along its lateral surface and tying the wire rings. The tubes used in this series of experiments were 3 centimeters in length and 2 centimeters in diameter (Fig. 1). Adult mongrel dogs were used for these studies. They were anesthetized with intravenous pentobarbital sodium. Under sterile conditions, the peritoneal cavity was exposed through an upper midline incision. After a hemigastrectomy had been carried out in the usual manner, the first part of the duodenum was mobilized, and a nylon prosthesis was fixed to its posterior surface by interrupted sutures between the serosal surface of this viscus and the nylon tube just beyond the folded seam. These sutures were all placed before any were tied, it having been found that any weakness in technique here would tend to predispose to separation. After these sutures had been tied, a continuous

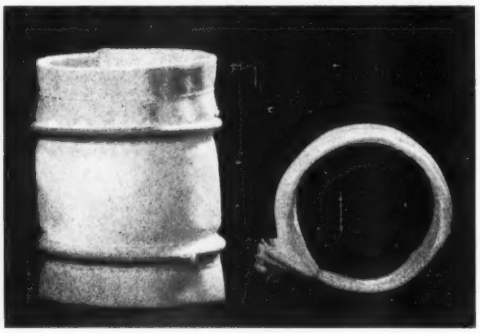

FIG. 1. Finished nylon tubes.

posterior suture was effected between the end of the tube and the mucosal surface of the duodenum in part of the animals. This was continued anteriorly as a Connell type suture. In some of the animals interrupted sutures of No. 4-0 silk were used for both layers. The final layer of the anastomosis was carried out by placing interrupted sutures between the serosa of the duodenum and the surface of the tube. After a portion of the gastric stoma had been closed, an anastomosis between the upper end of the tube and the stomach was completed in the same manner (Fig. 2). The omentum was then wrapped completely around the surface of the nylon tube and fixed with a few interrupted sutures. This step was considered necessary to forestall early leakage through the pores of the cloth. The same technique was used to interpose nylon tubes between segments of jejunum. The abdominal wall was then closed in layers without drainage, following which the animals were placed in their cages. No antibiotics were used in these experiments. The dogs were maintained on nothing by mouth for 3 days, after which water was allowed. On the sixth postoperative day regular kennel rations were given. These animals were followed for from 2 weeks to 8 months.

RESULTS

In the 9 dogs having nylon tubes inserted between the stomach and duodenum, 2 died from proximal suture line leakage (Table I). A diffuse peritonitis resulted from flooding of the peritoneal cavity by gastric content. Dog 5 died from distemper. His downhill course was abetted by occasional bouts of vomiting, during which time he aspirated gastric material. There was no evidence of leakage, as the entire "graft" was surrounded and effectively sealed by omentum. Reduction of the lumen of the nylon tube by about 75 per cent was reflected in gastric dilatation of a moderate degree. The fourth death

TABLE I.—EXPERIENCE WITH POROUS PLASTIC TUBES IN THE GASTROINTESTINAL TRACT

Dog No.	*Nylon tube substituted for segment of:*	*Period of observation, days*	*Result*	*Leakage*	*Findings at postmortem*
1	Pylorus and duodenum	244	Recovered	No	Nylon covered by omentum; no gastric dilatation
2	Pylorus and duodenum	2	Died	Yes	Diffuse peritonitis
3	Pylorus and duodenum	180	Recovered	No	Nylon covered by omentum; no gastric dilatation
4	Pylorus and duodenum	167	Recovered	No	Nylon covered by omentum; no gastric dilatation
5	Pylorus and duodenum	154	Died (distemper)	No	Nylon covered by omentum; moderate gastric dilatation
6	Pylorus and duodenum	152	Recovered (lost wt.)	No	Marked narrowing of nylon tube, advanced gastric dilatation
7	Jejunum	159	Died	Yes	Rupture of proximal suture line secondary to obstruction from trichobezoar in nylon tube; peritonitis
8	Jejunum	90	Recovered (lost wt.)	No	Stenosis in area of graft
9	Pylorus and duodenum	66	Recovered	No	Nylon covered by omentum; no gastric dilatation
10	Pylorus and duodenum	28	Died	Yes	Diffuse peritonitis
11	Pylorus and duodenum	55	Recovered	No	Nylon covered by omentum; no gastric dilatation

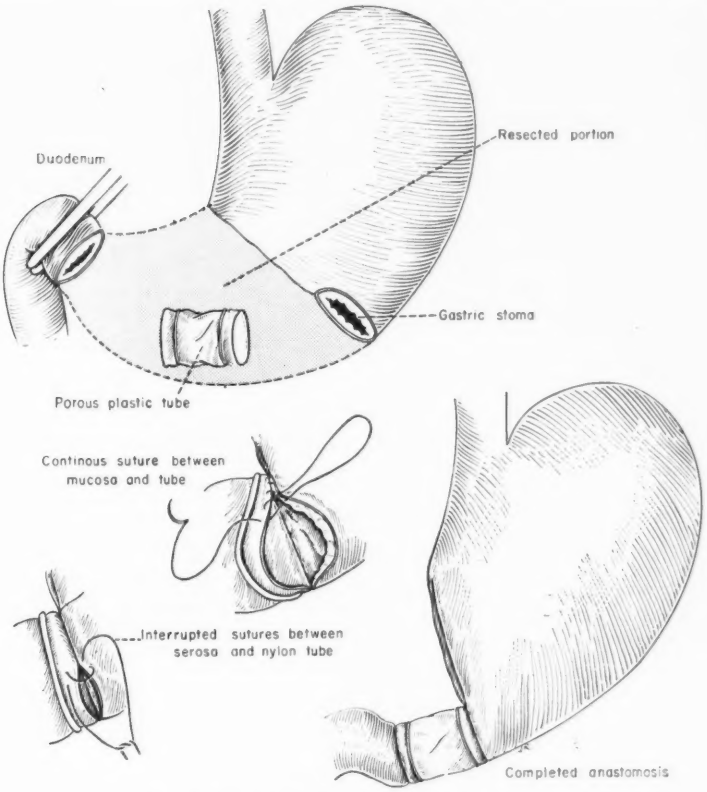

FIG. 2. Drawing illustrating implantation of tube.

occurred in an animal having a nylon tube inserted between two segments of jejunum. For 4 months this dog ate normally and maintained his weight. Then his course became progressively downhill until he died 158 days after operation. Postmortem examination revealed peritonitis, resulting from separation of the proximal suture line. The nylon tube had become obstructed by a trichobezoar as evidenced by a tightly packed hair ball within its lumen. Its bare inner surface was a graphic example of the failure of the gastrointestinal tract to form an epithelial lining of this material. Its outer surface was the site of a thick layer of fibrous tissue just under the omental covering. The nylon cloth could be separated from this fibrous tissue easily, as there was no evidence of its being incorporated within this sheath. The second dog's having a jejunal implantation of a nylon tube exhibited evidence of obstruction with gradual weight loss. When sacrificed, the "grafted" segment was found contracted with moderate proximal dilatation. When the fibrous sheath was opened, the nylon tube was partially detached at both ends and free within the lumen. Animal 6 maintained his weight for 2 months and then began to regurgitate with occasional aspiration. He was sacrificed 151 days after operation, at which time marked narrowing of the "graft" site was demonstrated. There was no ingrowth of tissue through the wall of the nylon tube; in fact, there was

FIG. 3.

FIG. 4.

FIG. 3. Mucosal surface of nylon tube 8 months after implantation between stomach (above) and duodenum.

FIG. 4. Appearance of fibrous sheath after removal of nylon tube.

necrosis and liquefaction of the tissue immediately adjacent to it.

The 5 remaining dogs maintained their weight without evidence of intestinal obstruction. After an 8 month period of observation, dog 1 was sacrificed. Upon opening the abdominal cavity, a generous amount of subcutaneous fat was apparent. There were no abdominal adhesions as evidenced by remarkable mobility of all viscera in the vicinity of the nylon prosthesis. Omentum was wrapped around its external surface, and it was firmly anchored to both the stomach and duodenum. A fibrous sheath measuring about 4 millimeters in thickness was demonstrated after removal of the omentum. Upon opening the prosthesis along with the stomach and duodenum, the inner surface of the cloth was found to be black in appearance and somewhat wrinkled (Fig. 3). Again, there was no inner lining and no evidence of an ingrowth of tissue through the wall of the tube. It was separated from the fibrous sheath without difficulty, leaving two transverse impressions from the wire rings. The bed from which the nylon tube was removed was red and friable, resembling granulation tissue (Fig. 4). Microscopic examination of this specimen near the upper anastomotic site revealed continuity between the outer surface of the fibrous sheath and the serosa of the stomach. The gastric musculature ended abruptly at the line of anastomosis, and no evidence of muscle tissue was left within the newly formed fibrous tube. A thin layer of epithelial cells was seen to extend from the gastric mucosa over the surface of the fibrous sheath (Fig. 5). A similar ingrowth of epithelium from the duodenum was also noted. Microscopic examination of the midportion of this sheath revealed many young fibroblasts and

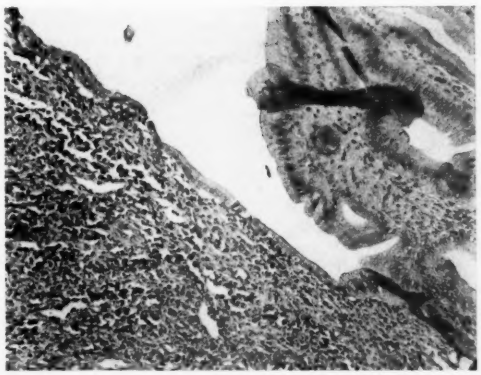

FIG. 5.

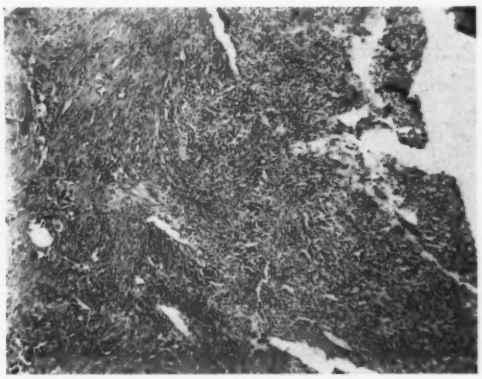

FIG. 6.

FIG. 5. Photomicrograph of junction between stomach (right) and fibrous sheath after 8 months. Epithelium is seen growing along surface of fibrous sheath.
FIG. 6. Photomicrograph of inner surface of midportion of fibrous sheath after 8 months.

newly formed blood vessels. Near the inner surface there was extensive infiltration by lymphocytes and plasma cells, while the outer portion revealed the deposition of a moderate amount of collagen. No epithelial lining was demonstrated in the midportion of the fibrous tube (Fig. 6).

Similar findings were observed in the 4 remaining animals.

DISCUSSION

After hemigastrectomy in the dog, it is possible to re-establish gastrointestinal continuity by means of a porous nylon tube with survival of the animal. A two layered anastomosis with interrupted nonabsorbable sutures is safer than one in which continuous catgut is utilized for the inner layer. Wire rings incorporated within the wall of the tube will prevent collapse as long as the suture line at each end remains intact. Five dogs survived for periods up to 8 months, maintaining their weight very adequately and without signs of obstruction. Unlike porous aortic substitutes, the epithelial lining of the gastrointestinal tract does not extend to cover the inner surface of the prosthesis. Moreover, the granulation tissue surrounding the tube does not permeate the pores of the cloth. Instead, the sheath remains loosely adherent to the nylon so that it lies more or less freely within this fibrous tube. This characteristic was well illustrated by an animal in which a 4 centimeter segment of the esophagus was replaced by a nylon tube containing 3 wire rings. Four months after operation, signs of progressive esophageal obstruction became more apparent. Re-exploration of this animal revealed the tube to have been passed from the esophagus. Only a fibrous stricture remained to identify the site of implantation. Epithelium from the two adjoining segments of the gastrointestinal tract was growing across the fibrous sheath but external to the nylon tube. Although it was not observed, the animals having gastroduodenal tubes probably would eventually have passed them if they had been followed for longer periods. This occurrence is invariably followed by contraction of the segment with stricture formation. These undesirable qualities of porous nylon tubes will limit their usefulness as substitutes for segments of the gastrointestinal tract.

SUMMARY AND CONCLUSIONS

1. It is possible to establish gastrointestinal continuity in the dog by means of a porous nylon tube with survival.

2. The cloth is not permeated by granulation tissue, nor is it lined by gastrointestinal epithelium.

3. Ultimately the tube is surrounded by a fibrous sheath, is detached from each suture line, and is passed from the animal.

4. Stricture formation with obstruction is a late development.

5. The mortality rate in this series was 35 per cent.

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KERATOACANTHOMA AS A SURGICAL PATHOLOGIC ENTITY

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PSEUDOEPITHELIOMATOUS HYPERPLASIA of the skin which occurs in response to chronic stasis ulceration, brominism, and diverse other stimuli has long been recognized. In recent years, interest has focused upon another and distinctive form of dermatologic epithelial hyperplasia, the keratoacanthoma, or molluscum sebaceum of European authors. Histologically, keratoacanthoma bears a striking resemblance to grade 1 epidermoid carcinoma of Broders, a diagnosis frequently conferred upon it. Patients with this benign disease have received therapy appropriate for carcinoma and have been incorporated into statistical studies of epidermoid carcinoma. This circumstance suggests the need for positive criteria to use in the diagnosis of keratoacanthoma and the value of reassessing the limiting boundaries of genuine epidermoid carcinoma of the skin.

The first reference in the English literature to keratoacanthoma appeared in 1936 when MacCormac and Scarff described a tumor which developed in 6 weeks on the cheek of a 67 year old woman. It consisted of an hemispheric nodule the size of a small nut clothed in normal skin except at its summit, where a slightly depressed adherent scale was noted. The scale peeled off with difficulty exposing a rough, irregular surface. Histologically, they observed a raised cyst with a lining of hypertrophic squamous epithelium, hyperkeratosis, and an ill-defined basal layer. The dermis was heavily infiltrated with inflammatory cells. In 10 similar lesions over a 10 year period, they implicated hypertrophic and inflammatory changes in a sebaceous cyst, or exposure to oils as possible etiologic factors. Superficial likeness to molluscum contagiosum suggested the name molluscum sebaceum which they applied to these tumors. The disorder has been variously labeled verrugoma by Gougerot, idiopathic cutaneous pseudoepitheliomatous hyperplasia by Grinspan and Abulafia, and molluscum pseudocarcinomatosum as proposed by a *Lancet* editorial (14). Rook and Whimster employ the term keratoacanthoma, the most acceptable designation at the present time. Subsequently, many reports have appeared which establish the entity as a relatively common, benign lesion.

In 1934, Dunn and Ferguson-Smith reported a case of multiple primary squamous cell carcinomas with spontaneous healing. Poth, in 1939, described similar self-healing "tumor-like" keratoses. Reports of comparable cases have followed. The disease is familial in character in some instances. A viral etiology is at times suggested on the basis of distribution of lesions. Actinic or oil sensitization has been implicated by some authors as a precursor.

Both the self-healing tumors and the keratoacanthomas are said to appear first as red papules. Individual lesions surge to their peak of development within a period of 6 to 10 weeks. The mature lesion is a raised, umbilicated nodule of 1 or more centimeters in diameter. Regional lymphadenopathy is rarely, if ever, present and the nodule is pulpy and moist as contrasted to the hard, dense consistency of a true epidermoid carcinoma. When fully evolved, the tumor remains stationary for a variable period of time and thereafter involutes by eversion and extrusion of its central keratinous core. The entire process ordinarily

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TABLE I.—COMPARISON OF PATHOLOGIC FEATURES OF KERATOACANTHOMA AND EPIDERMOID CARCINOMA

Gross	*Keratoacanthoma*	*Epidermoid carcinoma*
Size	Large	Usually small
Shape	Crateriform	Irregular
Color-cut surface	Yellow-tan	Gray
Consistency	Pulpy-moist	Hard-dense
Microscopic		
Adjacent epithelium-basal cells swollen and palisading lost	Characteristic	Uncommon
Epithelial downgrowths	Cohesive, rounded masses	Lack cohesion, pointed
Anaplasia	Absent	Present
Abnormal mitoses	Outnumber normal	Less common
Round red cell degeneration	Characteristic	Absent
Vacuoles	Common, compress nuclei	Absent
Basal cell layer	Absent	Locally absent
Inflammatory infiltrate:		
In epithelium	Marked	Scanty
Around epithelium	Heavy	Irregular
Spindle cell proliferation	Occasional	Infrequent
Fibrillar degeneration of collagen	Characteristic	Infrequent

occurs in less than 12 months, leaving a small depressed scar.

Several to hundreds of "self-healing" tumors have been observed on individual patients, usually over the seborrheic areas, and on the forearms and dorsa of the hands, and are characterized by an anamnestic, gross and histologic affinity to keratoacanthoma. Despite the conspicuous parallelism of individual lesions, multiple primary squamous cell carcinomas with spontaneous healing may represent a different clinical entity of greater destructive potential. Brown and Fryer believe the term self-healing epidermoid carcinoma to be fallacious and urge that it be discarded pending further observation.

OBSERVATIONS

Review of surgical files covering a 10 year period at Massachusetts Memorial Hospitals has disclosed 13 keratoacanthomas which were analyzed and compared to an equal number of low grade epidermoid carcinomas of the skin. Four keratoacanthomas had previously been diagnosed as epidermoid carcinomas. One lesion, at first thought to be a keratoacanthoma, was on re-examination considered to be an epidermoid carcinoma.

Ten keratoacanthomas were found in males; 3 in females, all of the white race. The average age at time of therapy was 66 years, ranging from 41 to 85 years of age. The sex and age distribution differed little from that of the epidermoid carcinoma group. Keratoacanthoma often arises in healthy skin, while concurrent premalignant or malignant disease of the skin is more conspicuous among patients with epidermoid carcinoma.

Most cases were biopsied or treated within 3 to 8 weeks of onset. The diameter of the lesions varied from 0.4 to 2.8 centimeters. In contrast, epidermoid carcinomas were often relatively smaller and had been present for longer periods of time.

Barring 1 patient with a history of creosote exposure and multiple epidermoid carcinomas of the skin, there were no significant occupational relationships or associated dermatologic ailments.

Nine keratoacanthomas were distributed about the eyelids, face, or neck. Three were located on the forearm or dorsa of the hands. One lesion was found on the penis. As far as one could determine from available records, the lesions were single and had not been preceded by other keratoacanthomas.

Investigation of available material has highlighted certain gross and histopathologic features of keratoacanthoma which are believed to constitute reliable diagnostic criteria and to distinguish this lesion from epidermoid carcinoma (Table I).

Grossly, keratoacanthoma is characteristically crateriform, with masses of keratin packed in centrally and superficially. The marginal uninvolved skin is stretched over the proliferating and keratinizing hyperplastic epithelium (Fig. 1). On section the mass is pulpy, moist, keratinaceous, exudes a cloudy fluid, and has a crumbling yellow-brown appearance. The smaller, hard, dry, usually gray, granular inlaid foci typical of epidermoid carcinoma are well known.

FIG. 1.

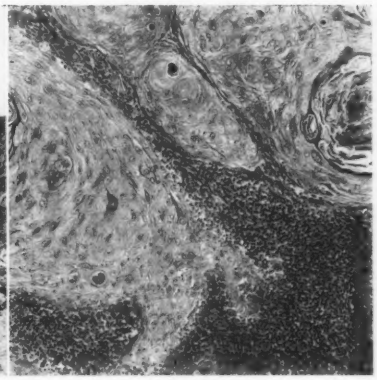

FIG. 2.

FIG. 1. The crateriform shape of a keratoacanthoma is shown, illustrating the central keratin mass, stretching of the uninvolved epidermis at the margin, and the surrounding inflammatory infiltration. All slides stained with hematoxylin and eosin. ×10.

FIG. 2. Hyperplastic rounded masses of keratinized epithelium, with pearls, are present surrounded by a heavy leucocytic exudate. Note the absence of anaplasia and of any recognizable basal cells. ×40.

Microscopically with low magnification both the hyperplastic and the adjacent uninvolved stretched epithelium have enlarged basal cell strata with swelling of individual cells, and a loss of the usual regular arrangement and palisading. Rounded masses of partly keratinized cells with abundant gound-glass-like eosinophilic cytoplasm and prominent intercellular bridges are bulging downward into the dermis and everting the marginal unaffected epithelium. Prominent hyperkeratosis and some parakeratosis are observed. The basement membrane boundary zones are obscured or lost, and a heavy infiltrate of leucocytes surrounds and overflows into the epithelial downgrowths (Fig. 2).

Carcinoma by contrast less regularly shows any alteration of the adjacent basal cells, the deeper lying epithelial masses are not so rounded, so rich in keratin, or so heavily infiltrated with and surrounded by leucocytes.

Under higher magnifications the diffuse mingling of leucocytes, particularly neutrophils, eosinophils, and lymphocytes, with the sheets of epithelium is further emphasized. Sometimes intraepithelial micro-abscess pockets of purulent exudate are present. Plasma cells, lymphocytes, and macrophages surround the epithelium in abundance (Fig. 3).

Degenerative cytologic epithelial changes are uniformly present and distinctive. Large empty cytoplasmic vacuoles in the keratinizing cells compress the nuclei into irregularly crescentic shapes. Similar vacuolar degeneration gives the epithelial pearls present a watery fibrillated appearance. Other individual cells are rounded, shrunken, necrotic, and stain an opaque dark red with a shriveled pyknotic or absent nucleus. This "round red cell degeneration," somewhat reminiscent of Darier's dyskeratotic corps ronds, is unusual in other hyperplastic and neoplastic proliferations (Figs. 4 and 5).

Locally spindle-cell appearances of the hyperplastic epithelium may be prominent in some instances. It is significant, however, that genuine anaplastic cytologic alterations like those of carcinomas are not present in keratoacanthomas (Fig. 6).

Mitoses are abundant in the hyperplastic epithelium, and abnormal mitotic figures with tripolar or multipolar appearance, or with chromosomal fragmentation and dispersion, usually outnumber the normal mitoses. (Figs. 7 and 8). In carcinoma, microscopically, the neoplastic epithelium is

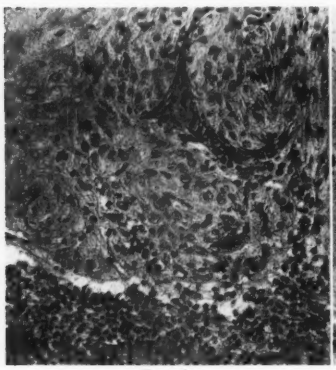

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 3. Leucocytes are illustrated around the hyperplastic epithelium of a keratoacanthoma, with localized epidermal infiltration, chiefly by lymphocytes and neutrophils. ×90.

FIG. 4. Cytoplasmic vacuolar degeneration is demonstrated in the cells of a keratoacanthoma, with local compression of the nuclei. ×545.

FIG. 5. A round degenerated red cell, as frequently observed in keratoacanthomas, is evident centrally as a black spheroid surrounded by a vacuole. Less marked dyskeratotic alterations are present in some of the adjacent cells. ×365.

not overrun with leucocytes, cytologic degeneration is absent or very localized, and normal mitoses predominate.

In the adjacent dermis, detached epithelial cells heavily infiltrated with leucocytes are found in keratoacanthoma. Here there is a fibrillar degeneration of collagen and elastic fibers, with an occasional foreign body giant cell reaction. The degenerative connective tissue changes with keratoacanthoma greatly exceed those that accompany epidermoid carcinomas of the skin.

DISCUSSION

Keratoacanthoma needs to be distinguished carefully both from carcinoma and from so-called pseudoepitheliomatous hyperplasia, if the concept is to have any validity. From the observations in the series reported and analyzed, distinction of keratoacanthoma from epidermoid carcinoma is based upon an absence of the reliable criteria of invasion and anaplasia upon which a pathologic recognition of cancers is usually based. Not only does the downgrowth of hyperplastic epithelium fail to invade the dermis in a convincing manner, but degenerative dyskeratotic alterations of the constituent epithelial cells are prominent, as indications of the abortive and self-limited nature of the tumor growth.

The distinctive cytologic degenerative epithelial changes are what set keratoacanthoma apart from other more nonspecific epithelial hyperplasias. Grossly the lesion mimics molluscum contagiosum, but lacks molluscum bodies. Microscopically the prominent cytoplasmic vacuoles and round red cell necroses of individual epithelial cells point to keratoacanthoma as a type of localized dyskeratosis. Predominance of abnormal mitoses is inferred to indicate a disturbance of nucleoprotein synthesis. Pseudoepitheliomatous hyperplasias lack the molluscum shape, the characteristic dyskeratotic abnormalities, and the evidence of disturbed nuclear metabolism by which keratoacanthomas are recognized pathologically.

In the uterine cervical epithelium, very similar microscopic changes have been termed "koilocytotic atypia" and equated with the pathologic term warty dyskeratosis. Here also such changes were not considered to indicate the presence of cancer.

The etiology remains obscure. Allen regards keratoacanthoma as a pseudoepithe-

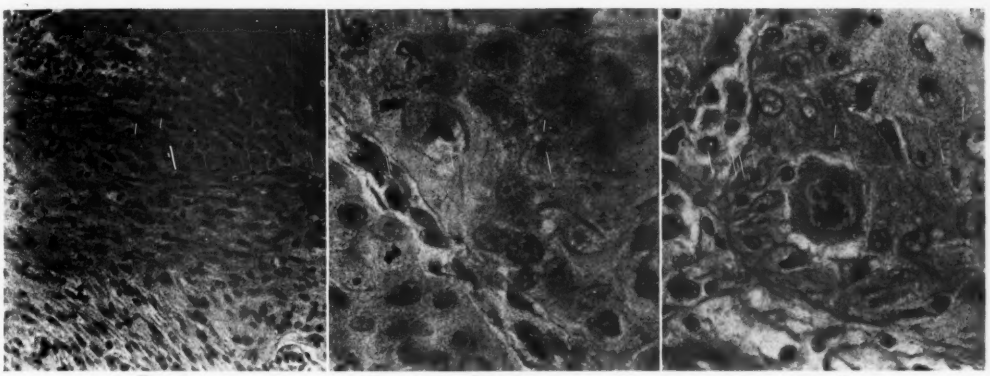

FIG. 6. FIG. 7. FIG. 8.

FIG. 6. Spindle cell proliferation found locally in an otherwise typical keratoacanthoma is not regarded as indicative of cancer. Note the abundant leucocytic infiltrate. ×90.

FIG. 7. Four abnormal mitotic figures, illustrating the clumping, dispersion, and bridging of the epithelial chromosomes found in the growing phase of keratoacanthomas. ×545.

FIG. 8. Another bizarre abnormal mitotic figure found in a keratoacanthoma. The fine black cytoplasmic granules might represent inclusion bodies, but they are not common or characteristic. ×545.

liomatous hyperplasia of the lining epithelium of epidermal inclusion cysts or coalescent comedones and states that inclusion cysts have a high incidence in these patients. Others believe the origin to be primarily in hair follicles.

Opinion is divided on the role of contact with oils, pitch, and tar. Binkley and Johnson categorized their patients into those of advanced age with no recognized etiologic factor, and into an industrial group composed of young males exposed to machine oil. Beare found only 1 pitch and tar worker in 76 cases. Mitze postulated as a probable cause the action of intense and repeated exposure to ultraviolet light on skin previously sensitized by tar and oil, emphasizing that most keratoacanthomas occur in exposed areas. He directed attention to the similar appearance of the tar papillomas and "carcinoids" of Rous and Kidd. The reported observation of Skirpan and Haserick of prominent cytoplasmic periodic acid Schiff positive granules in the cells of the stratum granulosum and squamous cell nests of keratoacanthoma, and the absence of such granules in overt carcinoma is particularly of interest.

An infective agent is postulated by many authors. Inclusion bodies have not been demonstrated by ordinary methods, and bacteriologic and mycologic investigations have been unrewarding. The age incidence and failure to accomplish transference by inoculation of filtrates does not support this hypothesis. A viral etiology is nevertheless suggested by the rapidity of development and involution of keratoacanthoma, and the not infrequent history of trauma preceding it. In cases in which lesions are multiple, the mode of spread and progression suggests autoinfection.

Ereaux inoculated the chorioallantoic membrane of the chick embryo with homogenized material from the skin lesions of 1 patient with multiple keratoacanthomas. Focal lesions were observed and reproduced through 5 consecutive passages. Electron microscopy revealed brick shaped particles smaller than, but similar to, the virus of molluscum contagiosum.

Barring Dupont, who reported local invasion in 6 of 28 cases, it is now generally accepted that keratoacanthomas are benign lesions which, left to themselves, will disappear in all cases. This opinion is sustained

by Calnan and Haber's review of 105 cases, 17 of which were allowed to involute spontaneously.

Keratoacanthoma has responded to curettage, radiation, and other forms of therapy. Local, total excision is the treatment of choice. It affords complete and instantaneous cure, maximum pathologic opportunity for excluding the presence of carcinoma, and satisfactory cosmetic results.

SUMMARY

Thirteen cases of keratoacanthoma, a benign self-resolving tumor entity of the skin of unknown etiology, are presented. Diagnostic criteria are discussed, and the gross and microscopic findings characteristic of this dyskeratotic lesion are considered. Total surgical excision is considered to provide the best treatment.

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THE USE OF NYLON PROSTHESES FOR DIAPHRAGMATIC DEFECTS

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LARGE HERNIAS and gaping defects may defy standard attempts at repair and reconstruction. Under such circumstances an additional substance must be incorporated in the reconstruction either to bridge the gap or to reinforce an otherwise tenuous repair. A variety of substances have been tried including muscle, fascia, skin, metallic meshes, and recently certain synthetic materials.

Although most attention has been directed to reconstruction of ventral and inguinal hernias, this problem is not uncommonly encountered in the diaphragm as a result of either congenital lesions or acquired defects related to trauma, excision of extensive tumors, and previous surgery. On the basis of our encouraging results with the use of the newer synthetic plastics within the body, this study was undertaken to evaluate a representative synthetic material, nylon, in the repair of defects of the diaphragm. To study the response to materials of different porosity, two widely different types of nylon were used—one, a mesh of widely spaced fibers and the other, a tightly woven fabric. The tolerance of each material in artificially induced infection is also presented.

MATERIALS

Nylon tulle (Fig. 1) was used to represent a widely porous, pliable synthetic material. Thread junctions were knotted (Fig. 1) which prevented slipping. A closely woven calendered[1] nylon fabric[2] was selected because of its comparatively minimal porosity (Fig. 1). This fabric has been shown to be impervious to the leakage of blood, except for a slight initial ooze, when used as a graft in the aorta in our laboratory (1, 4). Both forms of nylon were washed thoroughly with a commercial detergent in hot water to remove any soluble impurities. They were then sterilized by standard steam pressure autoclaving and wrapped in sterile towels ready for use.

METHODS

Mongrel dogs varying from 10 to 25 pounds were used. A total of 36 animals were equally divided; one-half had a hemidiaphragm resection and replacement by nylon net and the remaining group, by calendered nylon fabric. In 9 of each group of 18 animals the right diaphragm was replaced by each type of nylon prosthesis, and the 9 others were similarly treated on the left side. Intravenous pentobarbital sodium was used for anesthesia. Intermittent positive pressure was administered by a pneophore demand apparatus connected to an intratracheal tube.

Sterile technique was used throughout. The chest was entered through the ninth interspace on either side, and the lung was retracted to expose the diaphragm. From the midline laterally, the entire hemidiaphragm was resected except for a costovertebral margin of approximately 0.5 to 1.0 centimeter to which the nylon prosthesis was sutured. On the left side the crus of the diaphragm surrounding the esophagus was left intact. In 3 animals, however, the crus was also resected.

After the hemidiaphragm was resected the size of the remaining defect was measured, and a section of sterile nylon net or cloth

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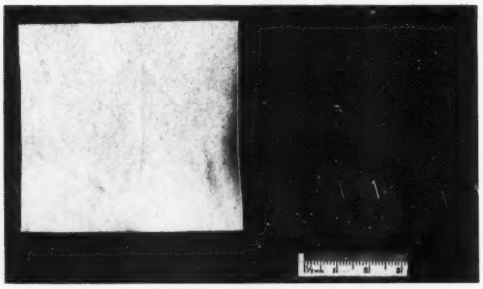
[1]Calendering, heat pressing between rollers, flattens the nylon threads resulting in a fabric of decreased porosity.

[2]This material has the following properties: thread count per inch, warp 254, filler 124; denier 70; air porosity 26.3; thickness 0.007 inches.



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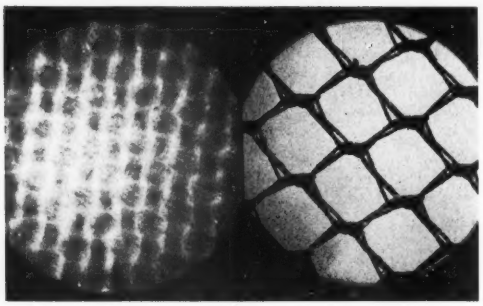

b

FIG. 1. Calendered nylon fabric (left), nylon net (right). a, Gross appearance. b, Photomicrograph, ×18 (description in text).

was cut to appropriate size. The nylon prosthesis was sutured to the remaining diaphragm margins with interrupted silk sutures. The lung was then expanded and the thoracic incision closed. Postoperatively the animals were placed on routine kennel diet and allowed to resume full activity. Daily penicillin was administered intramuscularly for 4 days.

Animals from each group with left and with right diaphragm replacements were sacrificed at specified postoperative intervals of 3, 7, 12, 18 days and 1, 2, 3, 6, 10 months. Fluoroscopic and x-ray examinations of selected animals were made prior to sacrifice.

Twelve rabbits were used to study the effects of infection upon the two types of nylon. Under pentobarbital sodium anesthesia the abdomen was shaved and covered with merthiolate solution 1:1,000. By semisterile technique a longitudinal skin incision approximately 5 centimeters long was made on each side considerably lateral to the midline to expose the underlying muscle surface. A 1 inch square piece of sterile calendered nylon fabric was sutured to the surface of the muscle sheath on one side and a square of nylon net of the same size similarly sutured on the opposite side. The nylon squares were held in place by 1 suture in each corner. The skin incision was closed with silk, but before tying the last suture a calibrated pipette was inserted into the wound to each nylon square. One cubic centimeter of a freshly prepared suspension containing 600 million virulent coagulase positive staphylococci per cubic centimeter was then ejected from the pipette into the wound. No antibiotics were administered, and the animals were permitted to resume normal activity. Abscesses and sloughing were allowed to progress and cultures were taken as indicated. The animals were electively sacrificed within a 2 week postoperative period.

RESULTS

Diaphragm replacements. At 3 days the underlying organs—liver and stomach—were loosely adherent to the nylon net and became more firmly attached by the end of 1 week. After 12 and 18 days small blood vessels occasionally were seen entering the interstices of the net along with fibrous tissue when the adherent organs were teased away (Fig. 2). The appearance from 1 month on remained essentially unchanged with liver and stomach adherent firmly at the line of suture between net and remaining diaphragm edge. One or both of these organs, varying with right or left sided prosthesis, were adherent to the net. Where the organs were not intimately adherent, the net was covered by a thin layer of fibrous tissue. On the superior surface of the nylon diaphragm the lung was seldom completely adherent except at the suture line. The remaining net surface was also covered by the thin film of fibrous tissue (Fig. 3). The net remained thin and pliable in all instances.

Of 18 dogs with nylon net prostheses all but 1 functioned well. This animal died (

FIG. 2. Dog No. 1473, 30 days. Close-up view of inferior surface of nylon net replacement of left diaphragm. Stomach, only partially adherent in this portion, has been retracted down to show ingrowth of blood vessels and fibrous tissue into net.

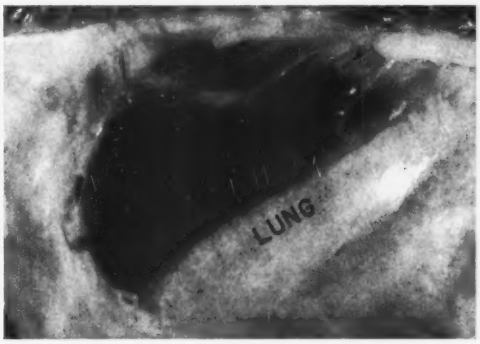

FIG. 3. Dog No. 1579, 6 months. Part of the superior surface of nylon net replacement of right diaphragm. The loosely adherent lung has been partially retracted down to expose the net covered by a thin translucent film of fibrous tissue. Adherent liver is visible beneath the net.

months postoperatively from a strangulated obstruction due to small bowel herniation through a 3 centimeter rent in the net. The reason for this tear was not apparent unless the net was accidentally traumatized in preoperative preparation and handling. One animal autopsied at 18 days had a left empyema adjacent to the net secondary to a wound infection. The exudate was mostly organized with the net intimately incorporated in the granulation tissue. In 1 other animal sacrificed just over 10 months postoperatively the liver appeared to have stretched the intact net slightly producing an appearance resembling a partial eventration. This might be explained partly by the marked weight change in this animal from 20 to 42 pounds. No other net exhibited this stretching phenomenon.

The calendered nylon fabric prostheses appeared to function less satisfactorily and to cause greater fibrous reaction. At 3 days parts of the fabric were covered by blood clot. As early as 1 week the cloth was considerably more rigid with small wrinkles. During the first month the cloth became incorporated in a progressively thickening layer of fibrous tissue. Direct fibrous growth into the fabric was observed. Older cloth prostheses tended to wrinkle and a number appeared to contract. One animal sacrificed at 4 months had a localized empyema with the fabric partially free and curled up in its center (Fig. 4). Another died approximately 3 months postoperatively from a strangulated obstruction due to bowel herniation through a separation of the suture line between cloth and diaphragm edge.

Histologically, the greater degree of reactive fibrosis about the calendered nylon cloth was striking. The fibrous tissue, however, did not uniformly infiltrate the fabric. The calendered nylon fabric frequently separated from the surrounding structures when attempts were made to cut sections with sharpened microtome blades. This problem was seldom encountered with the net prostheses.

In the animals selected for study by fluoroscopy and roentgenography the prostheses generally appeared to be satisfactory. The shadow cast by both net and fabric often resembled the contour of a normal intact diaphragm. There was no motion, however, except slight downward tipping of the medial part with inspiration due to pull of the opposite contracting hemidiaphragm.

Induced infection. Two of the 12 rabbits locally infected with virulent staphylococci died of an overwhelming septicemia. Three animals dislodged the calendered nylon patches from wounds by scratching. In the remaining 7 the cloth patches were found wrinkled or curled up in infected wounds

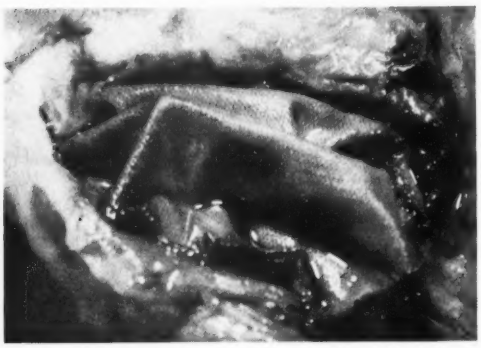

FIG. 4. Dog No. 1667, 4 months. Close-up view of calendered nylon fabric diaphragm replacement markedly wrinkled and partially free in localized empyema cavity. Parts of adjacent fibropurulent material have been removed.

(Fig. 5). At 2 weeks a thickened fibropurulent capsule usually surrounded the loose patch of nylon fabric.

In contrast to the calendered nylon, the net tolerated infection surprisingly well. There were less persistent infections and chronically draining sinuses. Five wounds separated and drained spontaneously. These rapidly became covered with granulation tissue that grew over the net and through the interstices. In 2, however, part of the net was loosened by scratching. In the remaining 5 animals the skin was completely healed and upon opening the wound the net was found in the original position grossly free of infection. In this situation a thin translucent film of fibrous tissue was found over the nylon net (Fig. 5). These wounds displayed remarkably little reaction to the injected staphylococci.

DISCUSSION

Nylon first attracted the attention of the medical profession by its use as a suture material. The sutures were shown to persist over long periods with no apparent change and with little tissue reaction. The strength and relative inertness of nylon led to its adaptation for such uses as joint linings and blood vessel replacements. The use of nylon to support tissue defects, however, has been centered largely on the repair of abdominal and inguinal hernias. Although sporatic reports have appeared in the foreign literature, this application of nylon has received little attention in this country.

The need for a satisfactory additional reinforcing material for the repair of hernias and tissue defects is attested to by the voluminous literature on the subject. Certain disadvantages accompany the use of autogenous tissues such as skin and fascia. Additional surgery is required, a limit exists on the amount of tissue available, and free grafts of both skin and fascia usually end up largely replaced by fibrous tissue.

The body has always reacted adversely to the presence of a foreign material. Impervious substances in the forms of plates or sheets are poorly tolerated when used for hernia repair. This was shown nicely in a recent study by Moore and Siderys in which nylon fabric was made impervious by fusion with nonporous polythene film. The body reaction to this nonporous material was characterized by excess fluid accumulation, marked fibroblastic reaction, and frequent suture line disruption. A significant advance was made by the introduction of metallic meshes. Tantalum mesh has had extensive trial but tends to undergo fragmentation with time. Koontz minimizes this feature by declaring that the surrounding fibrous tissue takes over the supporting function. Mesh of steel may not fragment but it still presents the disadvantage of rigidity. Metallic meshes may protrude through skin or erode into an adjacent viscus or blood vessel.

Partially as a side-product of current interest in the newer synthetic plastics for blood vessel replacements, several reports on the use of these cloth-like fabrics have appeared in the American literature on hernia repair. The fabrics whether nylon, orlon, fortisan, dacron, or polyvinyl sponge appear to function fairly well. Our findings also demonstrate a tendency for cloth-like fabric to wrinkle. This appears to be particularly evident if the material is not placed under proper tension. Perhaps the major disadvan

tage to the use of cloth-like fabric, however, is its poor tolerance in the presence of infection.

The ideal material would appear to be a tough, durable, inert, pliable, widely porous mesh or net that is tolerated in the presence of infection. Of the materials available to date, nylon net seems to be best suited to these requirements. Nylon net of the type used in this study has received trial mainly as a support for blood vessels or vascular grafts. The net generally functioned satisfactorily in this capacity but Deterling found dilatation in 3 net supported grafts 3 years after insertion into dog thoracic aortas. It was his feeling that the nylon fibers "fatigued" at the knots due to the continuous trauma of aortic pulsation. This type of stress is not present when the net is used for hernia repair.

Although metallic meshes have been used in the repair of hernias and eventrations of the diaphragm, the possibility of erosion into nearby structures such as the aorta, vena cava, esophagus, or lung exists. Such complications should not be present with the soft, pliable nylon net. When the net was used to bridge diaphragmatic defects in this study the underlying organs, usually stomach or liver, became largely adherent and probably served as the source for the fibrovascular infiltration of the net. Without an actual loss of diaphragmatic substance the net would also serve well to repair an eventration or to reinforce an otherwise weak hernia repair. The knotted fiber junctions permit tailoring to size and marginal suturing without fear of unraveling.

How well the nylon net prosthesis will hold up over a long time remains to be determined. Nylon has been shown to lose tensile strength when present in the body. It would appear, however, that its remaining strength would be adequate. The additional strength gained from surrounding fibrous tissue might possibly add further support. At present we are investigating another type of widely porous mesh that is stronger and excites a somewhat greater fibrous reaction.

FIG. 5. Abdomen of rabbit with incisions widely unroofed 2 weeks after infection with Staphylococcus aureus (see text). Calendered nylon fabric (left) curled up and loose with infection persisting. Nylon net (right) covered by thin film of fibrous tissue with no gross evidence of infection.

Whether this will be more desirable in the repair of defects subject to greater stresses than the net used in this study remains to be determined. We are also evaluating nets made from several of the other synthetic plastics that might maintain greater tensile strength. Perhaps eventually one may have available a number of different widely porous meshes of various plastics that could be adapted to reinforce various areas in the body needing support.

Nylon net may be used to repair hernias other than in the diaphragm. Our results to date, both experimental and clinical, would affirm its value in other locations such as abdominal and inguinal hernias and certain types of chest wall defects. Nylon net is tolerated directly under the skin without the troublesome prominence occasionally associated with tantalum mesh. Adjacent tissues should be in immediate contact with at least one surface of the net to serve as a source for fibrovascular infiltration. If a large sheet of mesh is used directly under the skin it is probably desirable to place a temporary subcutaneous drain to the net.

During the past year the nylon net has been used in 9 patients. Three had the repair of a ventral hernia reinforced by a sheet of nylon net. Four patients undergoing the

Urban type of radical mastectomy in which the second to fifth costal cartilages are completely resected had the costal defect bridged by nylon net. Two additional patients had sections of ribs resected in treating chest wall tumors. The net added stability and prevented paradoxic motion of the chest wall. One patient requiring resection of the lower costal cage and upper abdominal wall for removal of a chondrosarcoma developed a secondary infection. After draining the operative site and resecting a small centrally located loose portion of the net, the wound promptly healed. Granulation tissue could be seen growing over several areas of exposed subcutaneous net. In general the net appeared to function satisfactorily.

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CONGENITAL POSTEROLATERAL DIAPHRAGMATIC HERNIA IN THE NEWBORN

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RELATIVELY LITTLE has been published concerning the hazards and the operative management of congenital posterolateral diaphragmatic hernia in the early neonatal period. Indeed, Campanale and Rowland, reviewing the literature in 1955, stated that less than 6 cases had been reported in which operation was carried out under 48 hours of age.

Most of the larger reported series deal with somewhat older infants and, for this reason, fail to reflect accurately the over-all seriousness of this malformation. In this regard it should be noted that there is a marked dissimilarity in the clinical experience with this condition as portrayed in the reports from children's hospitals as compared with those from obstetric services. A relatively low children's hospital mortality in the management of diaphragmatic hernia is to be found in reports by Koop and Johnson, Gross, Riker, and Donovan. Potter (7), on the other hand, has stated that only 1 infant with diaphragmatic hernia born at the Chicago Lying-In Hospital has lived more than 6 hours. She believes that extrauterine respiration is never established in the majority of cases and that hypoplasia of the lungs is the principal cause of the early demise of these patients. The frequent occurrence of pulmonary hypoplasia also was suggested in the 1955 report of Campanale and Rowland. All 5 of their patients died. Three of them were operated upon, at ages of 45 minutes, 2 hours, and 21 hours. Two infants died without operation at 45 minutes and 3.5 hours of age. The authors found evidence of what they regard as pulmonary hypoplasia in all of these cases. In an excellent recent report from the Evanston Hospital, Bowers, McElin, and Dorsey have emphasized the importance of the role of the obstetrician in establishing an early diagnosis in cases of diaphragmatic hernia. Nine of the 13 infants with diaphragmatic hernia reported by them died within 2 hours of their birth and the diagnosis in these 9 cases was not made until postmortem examination was carried out. In all 4 cases diagnosed clinically the patients were operated upon and only 1 of these infants survived. This infant was 11 hours old at the time of operation. Thus, only 1 of the 13 infants born at their institution with diaphragmatic hernia survived.

The 13 cases reported by Bowers, McElin, and Dorsey were born at the Evanston Hospital during a 10 year period when there were 15,000 deliveries, an incidence of 1 case of diaphragmatic hernia in approximately every 1,200 births. Potter (8), in 1942, had encountered 10 cases of disphragmatic hernia at the Chicago Lying-In-Hospital during a period when there had been 21,000 deliveries. The frequency of occurrence of diaphragmatic hernia in these two studies is considerably higher than one might suspect from the relatively small number of cases reported in most series. Gross, for example, has reported the largest series of cases. However, his series from the Children's Hospital of Boston includes only 91 cases. He reports from the same institution 507 cases of imperforate anus, a malforma-

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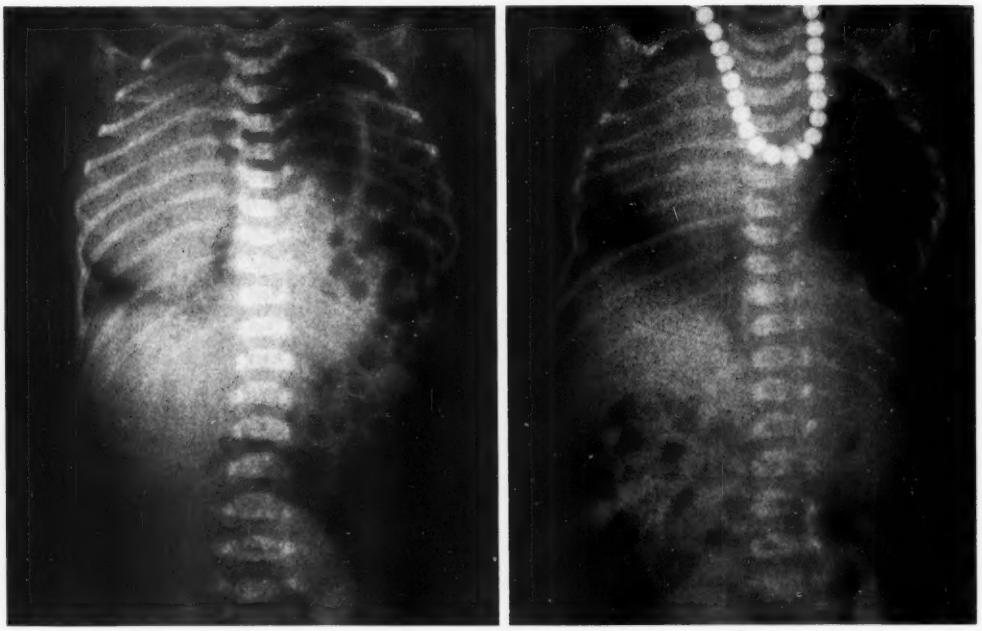


a b

FIG. 1. Roentgenograms of the chest in Case 3. a, 12 hours of age showing most of the left chest to be filled with intestines, upward compression of the aerated left lung, and mediastinal displacement into the right chest. b, After operation revealing incomplete expansion of the left lung with continuing, although less marked, displacement of the mediastinum and the heart into the right chest.

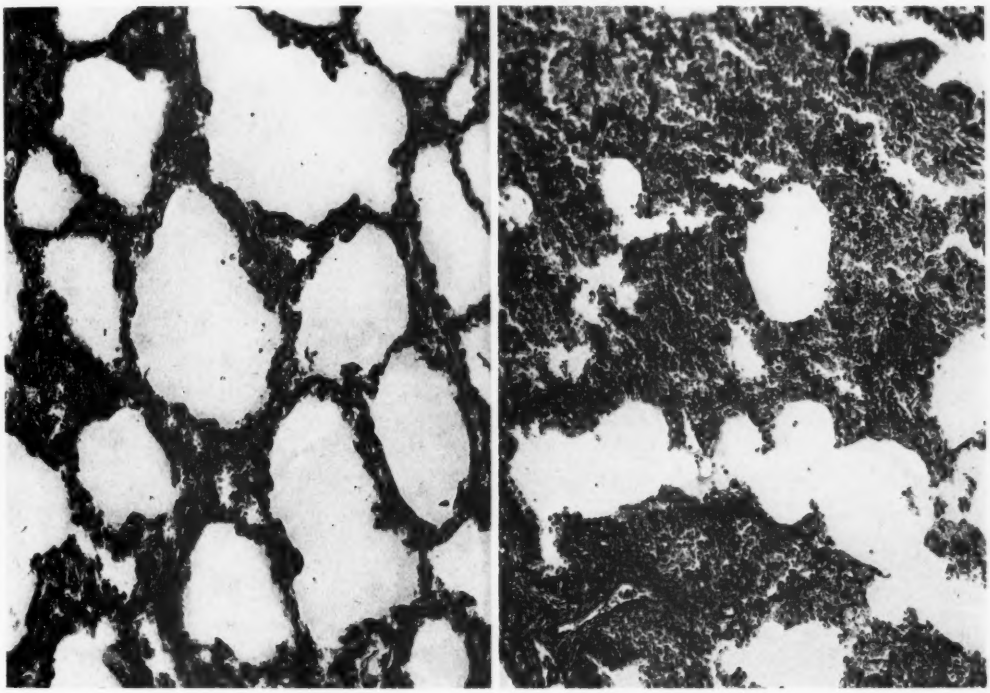
tion which statistically occurs somewhat less frequently, only once in every 5,000 births. Thus, the evidence at hand would seem to suggest that the majority of newborn infants with congenital diaphragmatic hernia die within the first few minutes or hours of life, often before a clinical diagnosis has been established.

Because of the limited reported experience with the operative management of diaphragmatic hernia in the early hours of life, it has seemed desirable to report 13 cases operated upon in the first 90 hours of life, 11 of them being under 40 hours of age at the time of operation. Reports of 3 additional cases in which the initial diagnosis was made at autopsy are included. The hernia was essentially of the posterolateral type and involved the left diaphragm in all of the cases. It should be noted that the great majority of patients with congenital diaphragmatic hernia who experience the onset of symptoms in the early hours of life have posterolateral defects which involve the left diaphragm.

CASE REPORTS

Cases Diagnosed Clinically and Managed by Operation

CASE 1. S. B., a white female, was born at the Ball Memorial Hospital on November 6, 1953. The pregnancy and birth had been normal. A large spina bifida with an 11 centimeter skin defect was found over the area of the lower thoracic, lumbar, and sacral spine. The heart appeared to be in the right hemithorax. The patient suffered from marked respiratory difficulty with cyanosis. Roentgenograms of the chest revealed the presence of a left diaphragmatic hernia. The patient was operated upon at 6 hours of age. An abdominal incision was made under endotracheal anesthesia. A large posterolateral defect in the left diaphragm was found. Virtually all of the abdominal viscera were in the left hemithorax. When the hernia was reduced, a small solid mass was found in the anatomic area which should be occupied by the hilum of the lung. The sma



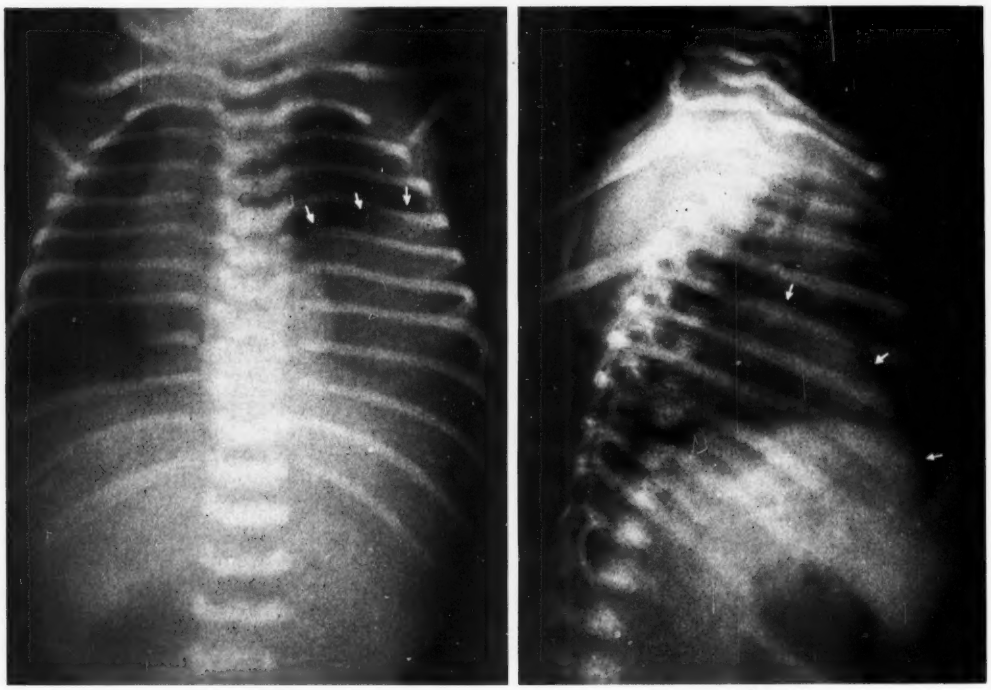
a b

FIG. 2. Photomicrographs of the right lung (a) and the left lung (b) of an infant whose diaphragmatic hernia was repaired at 14 hours of age (Case 3). The operator thought that there was agenesis of the left lung. The infant expired 24 hours after operation. Some areas of the right lung show atelectasis, while in other areas, such as the one pictured here, overdistention of alveoli and rupture of some alveolar walls is to be seen. In the left lung atelectasis predominates. Note the distended alveolar duct with collapsed alveoli about it. Alveolar structure is mature in both lungs. There is some distortion of alveolar pattern consistent with vigorous resuscitative efforts.

lung bud could not be expanded despite repeated efforts, and the infant remained quite cyanotic. The defect in the diaphragm was closed. Because of the inability of the peritoneal cavity to accommodate all of the viscera placed in it, only the skin of the abdominal incision was closed, creating a ventral hernia. However, the marked cyanosis remained unchanged and the infant expired 1 hour after operation. On postmortem examination, the heart and mediastinum were displaced into the right hemithorax, giving the appearance of a dextrocardia. The left lung was quite small and collapsed. The right lung was somewhat larger than the left and showed evidence of considerable atelectasis. The right lung weighed 18 grams and the left lung weighed 4 grams. On microscopic study, atelectasis was found to predominate in both lungs. Alveolar structure appeared mature bilaterally.

CASE 2. C. I., a white female, was born at the Indiana University Medical Center on March 23, 1956. The pregnancy and birth were normal. Dyspnea and cyanosis were noted shortly after birth. Roentgen examination of the chest revealed a left diaphragmatic hernia with displacement of the heart into the right hemithorax. The infant was operated upon at 12 hours of age. A left posterolateral diaphragmatic hernia was reduced, and the defect was repaired under endotracheal anesthesia through an abdominal incision. Some aeration of the left lung was obtained with pressure. No sac was found. Follow-up films of the chest taken 3 days after operation showed only about 50 per cent expansion of the left lung. She did well postoperatively and was discharged from the hospital on April 2. The left lung has expanded completely and the infant has continued to do well.

CASE 3. I. H., a negro female infant, was born at the Indiana University Medical Center on March 9, 1956. Polyhydramnios was noted during pregnancy. Delivery was normal. The infant weighed 5 pounds and 14 ounces at birth and was observed to have congenital dislocation of both hips. She was noted to be dyspneic

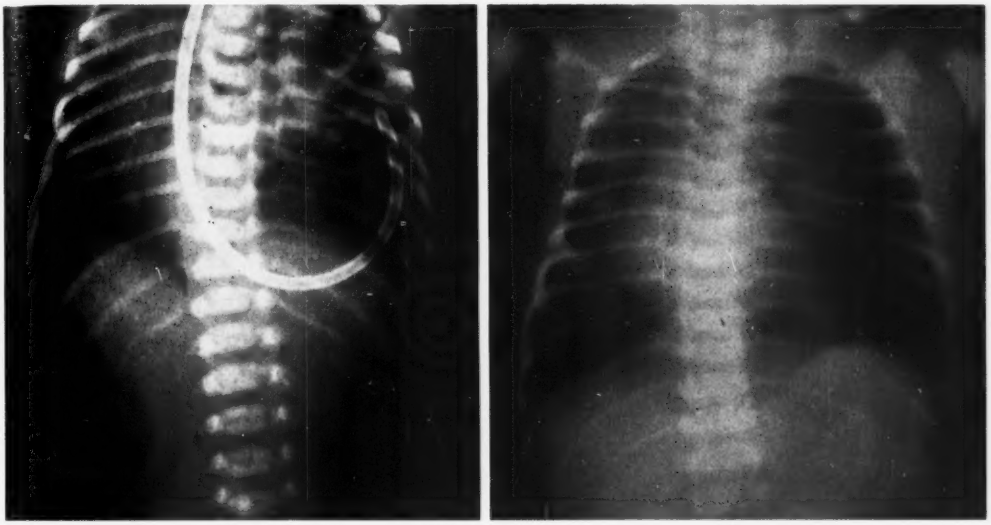


a b

FIG. 3. Chest roentgenograms in Case 4 taken 10 days after operation in the: a, posterior-anterior and, b, the lateral views showing excellent expansion of the left lung. The apparent elevation of the left diaphragm (arrows) was produced by the cyst of the peritoneal hernia sac. The heart is still displaced to the right.

and cyanotic following birth, and the heart appeared to be in the right hemithorax. A left diaphragmatic hernia was found on roentgen study of the chest. She was operated on through an abdominal incision under endotracheal anesthesia at 14 hours of age. A large left posterolateral diaphragmatic hernia was found with the bulk of the abdominal viscera in the left chest. The hernia was reduced. The operator felt that there was complete agenesis of the left lung. He was unable to identify any expandable left pulmonary tissue. The defect in the diaphragm was repaired and the abdominal incision was closed. Postoperative roentgenograms revealed incomplete expansion of the left lung (Fig. 1). The cyanosis and respiratory distress continued, and the infant expired 24 hours following operation. On postmortem examination, a large hernia sac was found to be attached to the superior surface of the left diaphragm. It protruded into the thorax and was filled with fluid. The left lung was markedly collapsed. There were a few small areas of aeration and crepitance. The right lung was small and contracted with many focal areas of atelectasis. In other areas, overdistention of alveoli with rupture of some alveolar walls was found (Fig. 2). Atelectasis predominated in the left lung. Alveolar structure appeared mature in both lungs. An interventricular septal defect was found on examination of the heart.

CASE 4. D. T., a white female, was born at the Ball Memorial Hospital on August 21, 1955. Resuscitation after birth was difficult and the infant remained cyanotic and dyspneic. The heart appeared to occupy the right hemithorax. Roentgenograms showed the left chest to be filled with abdominal viscera with the heart and mediastinum displaced into the right hemithorax. At 14 hours of age the infant was taken to the operating room. A left posterolateral diaphragmatic hernia was found and reduced through an abdominal incision. The large and small intestine, the spleen, the stomach and the left lobe of the liver were found to be in the left hemithorax. A Meckel's diverticulum also was discovered. No hernia sac was identified. A small solid mass could be palpated in the anatomic area of the hilum of the left lung. This could not be expanded by pressure through the endotracheal tube. The hernia defect was repaired and the abdominal incision was closed with interrupted silk sutures. A catheter which



a b

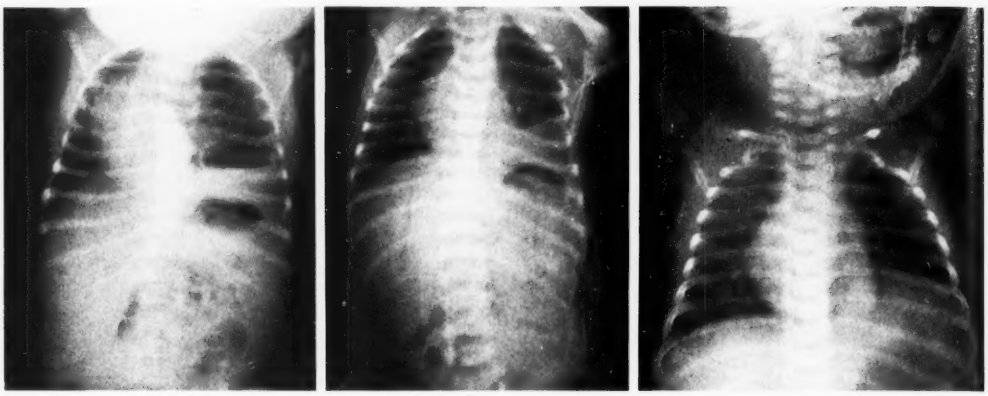
FIG. 4. Roentgenograms in Case 5. a, On admission to the hospital at 16 hours of age showing displacement of the esophagus and the mediastinum into the right chest and the displacement of the stomach (catheter) with the intestines into the left chest. b, There is partial atelectasis of right lung also. Film following operation demonstrating a left tension pneumothorax with complete collapse of the left lung and a right pneumothorax with partial collapse of the right lung.

was inserted into the left chest during repair of the defect was aspirated and withdrawn. The patient did well following operation, and increasing left pulmonary expansion was noted on frequent chest roentgenograms. Some emphysema of the right lung was noted immediately after operation. Twelve days following operation an area of increasing density was observed in the posterior aspect of the left diaphragm (Fig. 3). This condition did not produce symptoms, and therefore, the infant was released from the hospital on September 14.

The patient was readmitted to the hospital on October 27, 1955, in an exceedingly critical condition with a history of vomiting and abdominal distention of 3 days' duration. Evidence of small intestinal obstruction was found on roentgen examination of the abdomen. The infant's condition was improved somewhat by parenteral administration of fluids and electrolytes prior to operation. When the peritoneal cavity was opened, a midgut volvulus was found with gangrene and perforation of a large segment of the small intestine and generalized peritonitis. Resection of a large segment of the gangrenous small intestine was carried out. The infant died a few hours after operation. At autopsy, a large cyst was found to arise from the superior surface of the left diaphragm. This presumably was formed by the operative closure of the diaphragmatic defect in the presence of an unrecognized hernia sac. There was some atelectasis and pulmonary congestion bilaterally. The right lung weighed 40 grams and the left lung weighed 20 grams.

CASE 5. B. A., a 16 hour old white male infant, was admitted to the Indiana University Medical Center on March 23, 1956, because of dyspnea and cyanosis since birth with a roentgen diagnosis of left diaphragmatic hernia. The heart appeared to be displaced into the right hemithorax. On March 23, at 18 hours of age the patient was operated upon through an abdominal incision. Endotracheal anesthesia was used. A large left posterolateral defect in the diaphragm was found. The hernia was reduced and the defect was repaired. The left lung remained collapsed throughout the operation and could not be expanded with positive pressure. The infant remained cyanotic and dyspneic after operation. Postoperative roentgenograms showed a left tension pneumothorax with complete collapse of the left lung and a right pneumothorax with partial collapse of the right lung (Fig. 4). The patient expired 6 hours postoperatively.

On postmortem examination, the combined weight of the heart and lungs was 40 grams. The left lung was quite small and was almost completely collapsed and atelectatic. The left lower lobe contained a bleb which measured 2 by 2 centimeters. Focal atelectasis was noted throughout the right lung. Three blebs were found on the inferior surface of the right middle lobe. The largest of these blebs measured 1 centimeter in diameter. On microscopic study of both lungs, atelec-



a b c

FIG. 5. Roentgenograms of the chest in Case 6 taken: a, immediately after operation, b, 4 days following operation, and, c, 6 weeks following operation. In (a) there is air and fluid encysted in the hernia sac in the lower left chest and some obstructive emphysema of left lung. In (b), there is resorption of part of the air in the sac and a greater amount of fluid interposed between this and the gas bubble in the stomach. After the passage of 6 weeks, the air has disappeared, and the hernia sac remains as an opaque cystic shadow superadjacent to the left diaphragm.

tasis predominated and was most marked in the left lung. Focal areas of atelectasis and emphysema also were seen. The alveolar structure of both lungs appeared mature.

CASE 6. D. W., a 26 hour old white male infant, was admitted to the Indiana University Medical Center on September 15, 1956, because of cyanosis and respiratory difficulties. The pregnancy and birth had been normal. The infant was noted to have a grunting type of respiration and became quite cyanotic when out of the oxygen tent. The heart appeared to be in the right hemithorax on physical examination. Roentgenograms of the left chest demonstrated the presence of a left diaphragmatic hernia. The patient was operated upon at 28 hours of age through an abdominal incision. A large left posterolateral diaphragmatic hernia was found and repaired. No sac was identified at the time of operation. Moderate expansibility of the left lung was said to be observed. The postoperative course was uneventful. Roentgen studies following operation suggested that a sac had been present and had been converted into a diaphragmatic cyst by the closure of the defect (Fig. 5). Progressive expansion of the left lung with gradual return of the displaced mediastinal structures toward the midline was noted. The patient was discharged from the hospital on September 22.

CASE 7. D. A., a 24 hour old white male infant, was admitted to the Indiana University Medical Center on February 25, 1955, because of dyspnea, cyanosis, and a roentgen diagnosis of a left diaphragmatic hernia. The pregnancy and delivery had been normal. One sibling had died of congenital heart disease. Chest films confirmed the presence of a left diaphragmatic hernia, and the patient was operated upon at 30 hours of age. A large posterolateral defect in the left diaphragm was found through an abdominal incision. Marked cyanosis of the infant was noted on several occasions during the repair of the defect. At no time during the operation was the left lung seen. No sac was identified. The infant remained cyanotic and responded poorly. On postoperative roentgen study, the right lung appeared to be aerated. However, the left lung was completely collapsed with evidence of air in the left hemithorax under pressure. The infant died 9 hours following the operation. At autopsy, the left lung was found to be completely atelectatic. There was a marked shift of the heart and mediastinal structures to the right. The right lung was found to be largely atelectatic with some small areas of crepitation. Some alveolar ducts in atelectatic areas were found to be distended while their associated alveoli remained collapsed. The alveolar structure of both lungs appeared to be mature.

CASE 8. A. E., a 30 hour old white female infant, was admitted to the Indiana University Medical Center on January 2, 1956, because of dyspnea, cyanosis, and a roentgen diagnosis of left diaphragmatic hernia. The infant's temperature was 107 degrees Fahrenheit on admission. The pregnancy and delivery had been normal. Considerable difficulty had been encountered in resuscitating the infant after delivery. The patient was operated upon at 31 hours of age under endotracheal anesthesia. A large posterolateral defect in the left diaphragm was found through an abdominal incision. Virtually all of the abdominal viscera had herniated into the left hemithorax. The hernia was carefully reduced. The surgeon, on looking into the left thoracic cavity, was able to see a small bud of lung

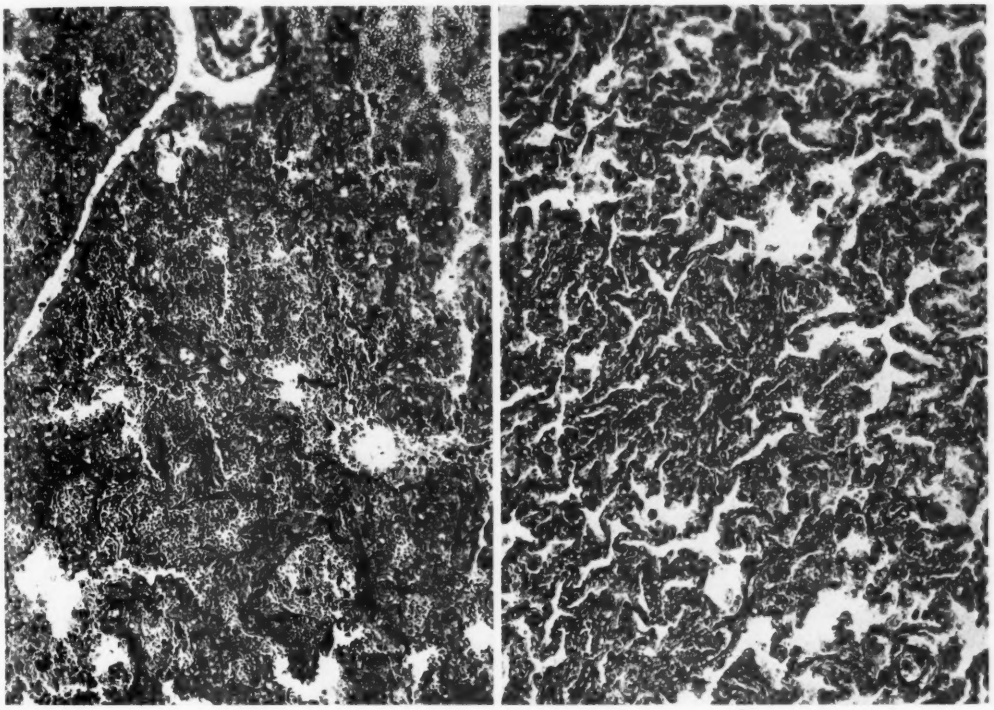


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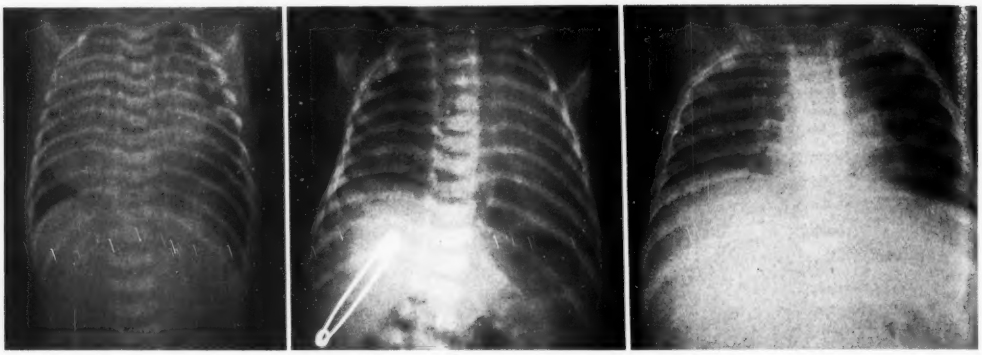
FIG. 6. Photomicrographs of the right lung (a) and the left lung (b) in Case 8. Hyaline membranes are found in the alveoli of the right lung. There is also an infiltrate of large mononuclear cells and red blood cells in the alveoli. The interstitial tissue also contains an infiltrate with mononuclear cells. The left lung, in this section, shows only slight expansion of the alveoli. There is no apparent involvement of the left lung with hyaline membrane disease. Alveolar morphology is quite distinct and structure appears mature in both lungs.

However, no expansion of this pulmonary tissue was observed. There was no evidence of a hernia sac. The diaphragmatic defect and the abdominal incision were closed. Chest suction was used following the operation. Postoperative roentgenograms showed failure of the left lung to expand and the presence of a left tension pneumothorax. The infant continued to have respiratory difficulty and expired 2½ days after operation. At autopsy, the left lung was atelectatic and dark red in appearance. The right lung was found to have some areas of crepitation with focal areas of atelectasis. Unilateral hyaline membrane disease, involving the right lung, was found on microscopic study (Fig. 6). The left lung was markedly atelectatic and free of hyaline membrane changes.

CASE 9. N. S., a 30 hour old white female, was admitted to the Indiana University Medical Center on February 13, 1955, because of dyspnea and cyanosis. The patient had been born without difficulty at the termination of a normal pregnancy. There were 3 normal siblings. The abdomen was soft and the heart appeared to be in the right hemithorax. The presence of a left diaphragmatic hernia was established by roentgen studies shortly after admission to the hospital. The patient was operated upon at 34 hours of age. A large left posterolateral diaphragmatic hernia was found and repaired through an abdominal incision. At no time throughout the procedure was the left lung visualized from below. Chest roentgenograms 7 days after operation revealed only partial expansion of the left lung. There was herniation of the overexpanded right lung through the superior and inferior mediastinum into the left chest. Some increased expansion of the left lung was noted on x-ray examination 15 days following operation. The patient was discharged from the hospital on March 3, 1955.

CASE 10. D. B., a 31 hour old white male, was admitted to the Indiana University Medical Center on August 3, 1951, because of dyspnea and cyanosis since birth. The infant would become quite cyanotic when



a b c

FIG. 7. Roentgenograms of the chest in Case 11 taken: a, on admission to the hospital prior to operation at 26 hours of age; b, 17 days following operation; and, c, 10 months following operation. The heart is still displaced into the left thorax due to collapse of the left lung in b. The film taken after 10 months shows re-expansion of the left lung.

out of the oxygen tent. The pregnancy and delivery had been normal. The heart appeared to be in the right chest. The presence of a left diaphragmatic hernia was confirmed by the roentgenograms and the infant was operated upon 1 hour after admission to the hospital, at 35 hours of age. A left thoracotomy incision was used. The bulk of the intestines, stomach, and spleen was found to have herniated into the left chest through a large posterolateral defect in the diaphragm. No sac could be found. The defect was repaired. The left lung had remained collapsed at all times and it could not be expanded at the close of the operation. The chest was closed without drainage. Virtually no expansion of the left lung was noted on daily roentgen studies of the chest for the first several days. A slow increase in expansion was noted thereafter. A fair degree of collapse still was detected 10 days following operation. The patient was released from the hospital on August 15. Outpatient roentgen studies on September 10, 38 days after operation, showed complete expansion of the left lung.

CASE 11. D. K., a 24 hour old white male infant, was admitted to the Indiana University Medical Center on March 23, 1948, because of dyspnea and cyanosis and a roentgen diagnosis of a left diaphragmatic hernia. Pregnancy and the birth had been normal. The heart appeared to be displaced into the right hemithorax. On March 24, at 39 hours of age, the infant was taken to the operating room. Through an abdominal incision, a rather large left posterolateral diaphragmatic hernia was found. The stomach and the large and the small intestines were in the left hemithorax. There was no hernia sac. The hernia was reduced and the diaphragmatic defect was repaired. The viscera could be replaced within the abdominal cavity with only the greatest amount of difficulty. For this reason, only the skin was closed. No mention was made of the degree of expansion of the left lung at the time of operation. The patient recovered and increasing left pulmonary expansion was noted on postoperative roentgen examinations (Fig. 7). The ventral hernia was repaired satisfactorily on April 13 and the infant was discharged from the hospital in good condition on May 4.

CASE 12. R. G., a 46 hour old white male, was admitted to the Indiana University Medical Center on February 25, 1951, because of dyspnea and cyanosis since birth. The patient had experienced some difficulty in beginning respirations after delivery. The pregnancy and labor had been normal. On physical examination, the heart appeared to be in the right chest. Roentgenograms confirmed the presence of a left diaphragmatic hernia. The mediastinal structures were displaced to the right. The infant was taken to the operating room at 62 hours of age. The left posterolateral hernia was reduced and the defect was repaired through a thoracic incision under endotracheal anesthesia. No sac was found. The defect was a relatively small one and it had to be enlarged to permit reduction of the hernia. The left lung appeared to be atelectatic at the time of operation and only a small amount of expansion could be achieved even with considerable pressure being exerted through the endotracheal tube. Increasing left pulmonary expansion was noted on repeated postoperative roentgen studies. The postoperative course was relatively uneventful and the patient was discharged from the hospital on March 11.

CASE 13. M. W., a 72 hour old white female, was admitted to the Indiana University Medical Center on January 10, 1950, because of dyspnea and mild cyanosis. The pregnancy and delivery had been normal. The heart appeared on examination to be in the right hemithorax. Roentgenograms taken on admission to the hospital showed a left diaphragmatic hernia with displacement of the heart into the right chest. The p-

tient was operated upon at 90 hours of age on January 11. A posterolateral diaphragmatic hernia was reduced and the defect was repaired under endotracheal anesthesia through an abdominal incision. No mention in the operative record could be found of difficulty with left pulmonary expansion. The postoperative recovery was prompt and postoperative roentgen studies showed progressive re-expansion of the left lung. The infant was discharged from the hospital on January 24.

Cases Diagnosed at Autopsy

CASE 14. I. B., a white female weighing 8 pounds and 5 ounces, was born at the Indiana University Medical Center on April 15, 1948. The pregnancy and delivery had been normal. The heart was noted to be in the right hemithorax. Attempts at resuscitation produced no apparent oxygenation. The infant remained cyanotic and expired 45 minutes after birth. A large left posterolateral diaphragmatic hernia without a sac was found on postmortem examination. The left chest was filled with abdominal viscera and the heart and mediastinum were displaced into the right hemithorax. This displacement had caused considerable compression of the right lung. The right lung weighed 13.5 grams. The left lung was quite small, measuring only 1.5 centimeters in its greatest length. It weighed only 2.2 grams and appeared nonaerated (Fig. 8). Indeed, the only aerated pulmonary tissue to be found was a small patch of pink lung parenchyma in the base of the right lung. On microscopic examination of the lungs, atelectasis was found to predominate (Fig. 9). Occasional, scattered areas of aeration were encountered. All of the lung tissue studied appeared to be mature in development. No other congenital malformations were found.

CASE 15. M. D., a white female weighing 6 pounds and 3 ounces, was born at the Indiana University Medical Center on August 22, 1953. The pregnancy and delivery had been normal. The infant remained cyanotic despite vigorous efforts at resuscitation. She was placed in an oxygen crib and failed to improve. She died 2 hours after birth. At autopsy, a large left posterolateral diaphragmatic hernia without a sac was found. The left chest was filled with abdominal viscera which compressed the left lung against the vertebral column. The left lung was quite small and atelectatic in appearance. It sank in water. The right lung was only slightly smaller than normal and appeared to be partially expanded. The right lung floated in water. The microscopic appearance of the pulmonary tissue was principally one of atelectasis. Only occasional expanded alveoli, at times emphysematous, were found. Coarctation of the aorta and left ureteral stenosis with hydroureter and hydronephrosis also were discovered.

CASE 16. C. S., a white female weighing 6 pounds and 15 ounces, was born at the Indiana University Medical Center on July 8, 1954. The pregnancy and delivery had been normal. Dyspnea and cyanosis were noted at birth. The infant was placed in an oxygen incubator and her color and respirations improved somewhat. However, within a short time her dyspnea and cyanosis again became marked and she expired at 6 hours of age. A moderate sized left posterolateral diaphragmatic hernia without a sac was found at autopsy. The left chest was filled with abdominal viscera and the heart and mediastinum were displaced to the right. The left lung was small and atelectatic in appearance. The right lung weighed 26.7 grams and the left lung weighed 10 grams. On microscopic examination, considerable atelectasis was encountered. There was a marked decrease in the number of air-containing alveoli with overdistention of small areas of alveoli. One section of lung showed complete absence of air-containing alveoli. No other congenital abnormalities were found.

DISCUSSION

The 3 cases of diaphragmatic hernia diagnosed at autopsy are recent ones and do not represent the entire experience of the Indiana University Medical Center with this type of case. It is likely that a relatively significant incidence of diaphragmatic hernia may be found in institutions where all neonatal deaths are investigated by postmortem examination. In this regard, it is of interest that 38 cases of diaphragmatic hernia in infants were discovered in the autopsy files of the Department of Pathology of the University of Minnesota in 1942 by Haugen and Ehrenberg. Potter (8), in 1942, had discovered 70 cases of diaphragmatic hernia in a series of 1,700 autopsies on infants and fetuses born with malformations. Fifty-three of the infants in this group were liveborn and 17 were stillborn. Ten of these infants had been born at the Chicago Lying-In Hospital.

In the 4 youngest infants operated upon in our series, diagnosis and operation were performed in the institution of their birth, the Indiana University Medical Center or the Ball Memorial Hospital. All 9 of the older infants who were managed by operation were transferred to the Indiana University Medical Center from other hospitals.

The characteristic diagnostic triad observed in all of these infants in whom clinical diagnosis was made in the early hours of life was one of dyspnea, cyanosis, and "dextrocardia." The "dextrocardia" appeared to

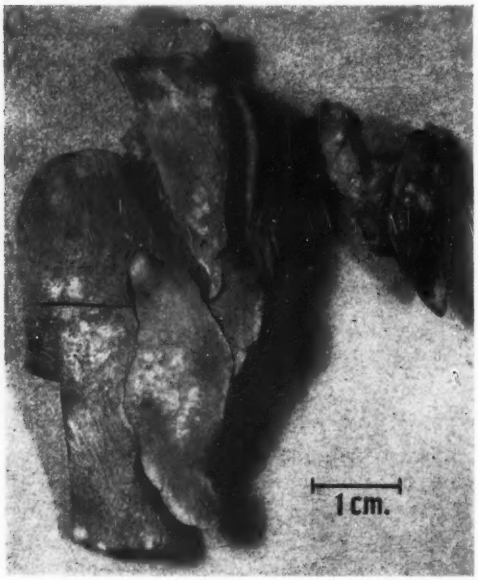


FIG. 8. Photograph showing the postmortem appearance, after fixation in formalin, of both lungs in Case 14. The marked difference in the size of the two lungs is quite apparent. The left lung weighed only 2.2 grams at autopsy, whereas the larger right lung weighed 11.2 grams.

be the most notable physical finding in these cases, and several of these infants were referred to the hospital with suspected congenital cyanotic cardiac disorders with "dextrocardia." The appearance of "dextrocardia" was due to the mediastinal displacement produced by the diaphragmatic hernia and often persisted for several days, to a progressively reduced degree, after operative reduction of the hernia and repair of the diaphragmatic defect.

In all of the cases in this series, both clinical and autopsy, the hernia defect involved the left diaphragm and was essentially of the posterolateral, foramen of Bochdalek type. The hernia defects in these cases tended to be rather large and permitted the herniation of a significant portion of the abdominal viscera into the left chest. A sac seldom was present. It was found in only 3 of the 16 cases in this study.

All but 2 of the 13 patients who were managed by operations were operated upon under 40 hours of age. An abdominal incision was utilized in 11 cases and in 2 cases a transthoracic approach was employed (Table I). A hernia sac was not found at the time of operation in any of the patients. However, the presence of a sac subsequently was established in 3 of the cases. Eight of the infants recovered and 5 died. The operative mortality was highest among those infants who were operated upon at earlier ages. In addition to the diaphragmatic defect and the accompanying abnormal midgut rotation and fixation which permitted the bulk of the midgut to occupy the left hemithorax, 5 of the 16 infants were found to have other congenital malformations (Table II). One of the patients (Case 4) survived operative repair of the diaphragmatic hernia but died at 2 months of age of midgut volvulus, gangrene, and perforation with generalized peritonitis.

The expansibility of the left lung during the early hours of life in these infants is of considerable interest. A clear statement concerning the observed expansibility of the left lung at the time of operation was contained in the operative notes of 11 of the 13 cases managed by operation. In 8 of the cases, the left lung was found to be small and collapsed and no expansion whatsoever of the left lung could be obtained. Endotracheal anesthesia was employed in all cases. This lack of expansibility was observed despite the rather vigorous utilization of positive pressure in some instances. Minimal expansion of the left lung was noted in 2 cases and moderate expansion in 1. The left lung was found to be small and atelectatic in all 8 of the cases in which postmortem examination was carried out during the early hours after birth. In those cases in which the lungs were weighed separately, the left lung weighed significantly less than the right. Atelectasis predominated on microscopic examination and was most marked in the left lung. There were scattered areas of significant emphysema in some cases and, in a few instances gross emphysematous blebs were discovered at autopsy. Although the effect of this ante

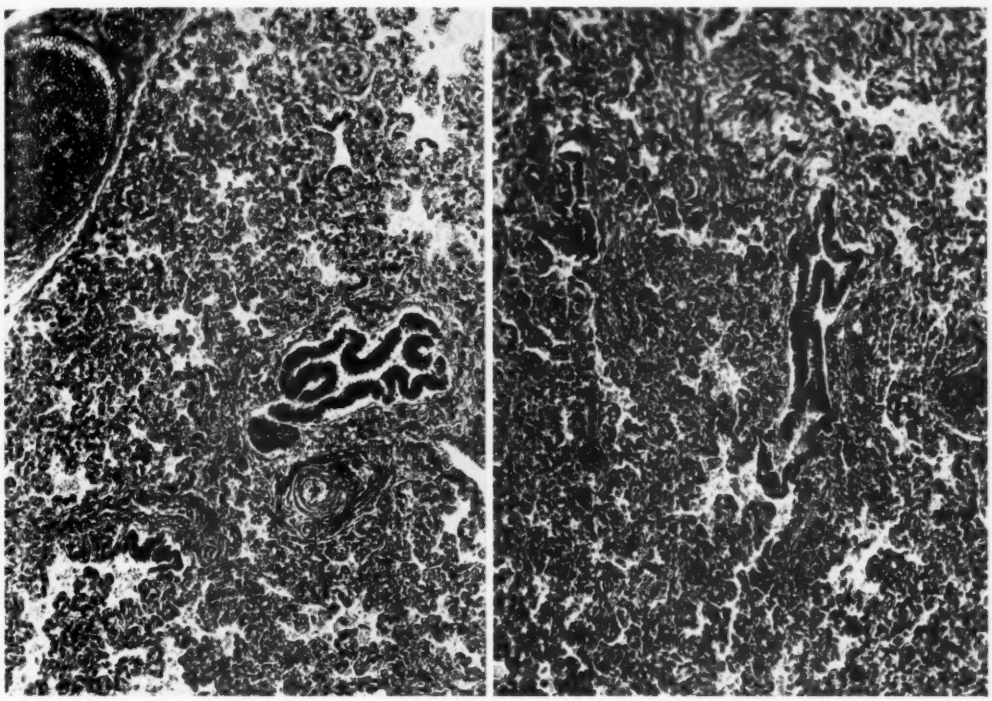


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FIG. 9. Photomicrographs of the right lung (a) and the left lung (b) in a newborn infant (Case 14) with a left diaphragmatic hernia who died 45 minutes after birth. Both lungs show atelectasis, the left more than the right. There is no significant difference in the morphology of either lung. The pulmonary tissue otherwise appears to be mature.

natal compression collapse of pulmonary tissue and its accompanying limitation of pulmonary expansibility was observed to be marked in the left lung, some involvement of the right lung to a lesser degree also was found. In all of the cases in which pulmonary tissue was available for microscopic study, the alveolar structure was observed to be mature.

The discovery of unilateral hyaline membrane disease of the lung in 1 case (Case 8) is also of interest. This observation may be of some aid in evaluating some of the possible etiologic factors which have been cited as influencing the production of pulmonary hyaline membrane disease in the newborn. The hyaline membrane disease in this case was found to involve the expanded right lung, while the collapsed and never expanded left lung was completely free of the pathologic changes characterizing this disease. This finding might be regarded as lending support to those theories which suggest that this disorder results from direct contact of the expanded alveolus with some potentially noxious substance which had passed into it through the tracheobronchial tree. It is possible that the continuing collapse of the never expanded left lung kept some noxious substance from coming into contact with the alveoli of this lung.

Roentgen studies which were carried out on those patients who survived operation showed a slow but progressive expansion of the left lung and a gradual correction of the marked preoperative displacement of the heart and mediastinum into the right hemithorax. This was observed even in those

TABLE I.—SUMMARY OF EXPERIENCE WITH 13 CASES OF LEFT POSTEROLATERAL DIAPHRAGMATIC HERNIA TREATED DURING THE EARLY NEONATAL PERIOD BY REDUCTION AND REPAIR OF HERNIA

Case No.	*Year*	*Sex*	*Age at time of operation, hours*	*Presence of sac*	*Operative approach*	*Expansibility of left lung at operation*	*Result*	*Remarks*
1	1953	F	6	No sac	Abdominal	None	Died	Death 1 hour following operation
2	1956	F	12	No sac	Abdominal	Minimal	Recovered	Progressive increase in expansion of left lung on postoperative roentgen studies
3	1956	F	14	Sac*	Abdominal	None	Died	Death 24 hours following operation
4	1955	F	14	Sac*	Abdominal	None	Recovered	Roentgen evidence of increasing expansion of left lung postoperatively. Death at 2 months of midgut volvulus with gangrene and peritonitis
5	1956	M	18	No sac	Abdominal	None	Died	Death 6 hours following operation
6	1956	M	28	Sac*	Abdominal	Moderate	Recovered	Progressive expansion of left lung
7	1955	M	30	No sac	Abdominal	None	Died	Death 9 hours following operation
8	1956	F	31	No sac	Abdominal	None	Died	Death 2.5 days after operation. Temperature 107 degrees on admission. Atelectasis on left and unilateral hyaline membrane disease (on right) at autopsy
9	1955	F	34	No sac	Abdominal	None	Recovered	Slow but progressive expansion of left lung on postoperative roentgenograms
10	1951	M	35	No sac	Thoracic	None	Recovered	Slow increase in expansion of left lung on roentgen studies following operation
11	1948	M	39	No sac	Abdominal		Recovered	Progressive postoperative expansion of the left lung
12	1951	M	62	No sac	Thoracic	Minimal	Recovered	Roentgen evidence of increasing expansion of the left lung noted postoperatively
13	1950	F	90		Abdominal		Recovered	Progressive postoperative expansion of the left lung on roentgen study

*Although the sac was not found at the time of operation, its existence subsequently was demonstrated. The sac had been converted, by the hernia closure, into a cyst arising from the superior surface of the diaphragm at the site of the hernia defect.

cases in which the left lung was found at operation to be collapsed, small, and nonexpansible. From these observations, it would appear that the capacity of the collapsed and nonexpansible left lung slowly to expand is established. However, a number of days and even weeks may be required to complete the effective expansion of this lung.

To describe the ipsolateral pulmonary changes in these cases simply as hypoplasia may be somewhat misleading. The precise meaning of hypoplasia with respect to pulmonary changes at birth is not entirely clear and the use of this term to describe alterations in the ipsolateral lung accompanying congenital diaphragmatic hernia recently has become rather controversial. Possibly some descriptive term such as antenatal compression atelectasis may prove to be more useful. This term would be used to characterize the lung, which is small, collapsed, and nonexpansible but which, with the passage of time, may be expected slowly to expand and assist in supporting life if the infant survives. It should be understood that this antenatal compression type of atelectasis differs from the "acquired" type involving a once expanded lung in that removal of the compression will not necessarily be followed by prompt expansion and function of the involved lung or pulmonary segment.

The vigorous use of positive pressure through the endotracheal tube at the time of operation in an attempt to expand one of these small and nonexpansible lungs must be avoided. These lungs cannot be expanded by this type of effort and only harm can result. The already expanded alveoli become overdistended and may rupture. In 1 of our patients (Case 5) bilateral pneumothorax presumably resulted from the rupture of emphysematous blebs which were produced by the use of excessive positive pressure. Attempts to expand these lungs following operation through the vigorous use of chest suction are equally ill-advised.

An abdominal incision was utilized by preference in the majority of cases and is regarded as the more suitable of the two operative approaches. The creation of a ventra

TABLE II.—SUMMARY OF AUTOPSY FINDINGS IN INFANTS DYING DURING THE NEONATAL PERIOD

Case No.	*Sex*	*Operated upon*	*Age at death*	*Weight of infant, grams*	*Measurement of lungs**	*Left lung*	*Additional malformations†*
1	F	Yes	7 hours	3880	Right lung—18 grams; left lung —4 grams	Small and atelectatic	Spina bifida
3	M	Yes	38 hours	2740	Both lungs 25 grams	Small and atelectatic	Interventricular septal defect. Congenital dislocation of both hips
5	M	Yes	24 hours	3260	Heart and both lungs 40 grams	Small and atelectatic	
7	M	Yes	39 hours	3693	Heart and both lungs 65 grams	Small and atelectatic	
8	F	Yes	4 days	2352	Heart and both lungs 50 grams	Small and atelectatic	Cysts of the right kidney
14	F	No	45 minutes	3750	Right lung—11.3 grams; left lung 2.2 grams	Small and atelectatic	
15	F	No	2 hours	2730		Small and atelectatic	Stenosis of left ureter with hydroureter and hydronephrosis. Coarctation of the aorta
16	M	No	6 hours	3090	Right lung—26.7 grams; left lung —10 grams	Small and atelectatic	

*The weight of the lungs in newborn infants weighing from 2250 to 3250 grams ranges from 49.5 to 54.7 grams and the weight of the heart ranges from 17.9 to 20.1 grams (9).
†In 1 other infant (Case 4), a Meckel's diverticulum was discovered at the time of operation.

hernia through the approximation of only the skin of the abdominal incision was necessary in 2 cases (Cases 1 and 11) because of the inability of the abnormally small celomic cavity to accommodate the viscera with the muscle layers of the abdominal wall intact.

An additional problem encountered in these infants operated upon during the early hours of life concerns the failure to recognize the presence of a hernia sac at the time of operation. This occurred in 3 of our patients. When the lung is small and cannot be expanded at operation, the sac remains closely approximated to the collapsed lung by the negative intrathoracic pressure and cannot be easily identified. One possible solution to this problem might be to make a small intercostal incision into the lower left chest after the peritoneal cavity had been entered. In those cases in which the diaphragmatic defect is a relatively large one, a small incision in the pleura of the chest wall from inside through the diaphragmatic defect may be preferable. The small pleural opening with the introduction of air into the left pleural space would permit a sac, if present, to fall away from the collapsed and nonexpansible left lung. The sac then could be more easily identified and at least partially excised in order to avoid the creation of a large cyst on the superior surface of the diaphragm as occurred in 3 of our infants. It should be noted that the presence of a sac may be suspected on roentgen examination if some aerated lung is seen in the superior portion of the left hemithorax.

There is clearly a great need for improvement in the results of the management of congenital diaphragmatic hernia. Since so many of these infants die during the first minutes and hours of life, the attack on this problem through earlier diagnosis must, of necessity, be directed by the obstetricians. In this regard, it would seem desirable that immediate roentgenograms of the chest during the early minutes of life be made in all cases in which a newborn infant does not breathe easily and spontaneously after delivery. If more of these infants are to be salvaged, the operative attack on this problem must come earlier rather than later as suggested recently by Roe and Stephens. Although the statistical results of delayed operation can be expected to be better than those of early operation, this result comes about largely through an unfortunate process of

case selection resulting from the demise of a significant number of the poor risk patients. While the evidence at hand suggest that operation cannot be advocated on grounds of permitting prompt pulmonary expansion and function on the involved side, early reduction and repair of the hernia will create the optimum conditions for the gradual expansion and function of the lung which may be found at operation to be collapsed and nonexpansible. It is possible that delay of operation in some cases may lead to some increase in pulmonary compression by distention of the intrathoracic stomach and intestines with swallowed air. The combination of early diagnosis and repair of the hernia with the use of some means of artificial oxygenation of the blood, until the capacity of the infant's respiratory mechanisms to support life have become established, may ultimately prove to be the solution to this exceedingly difficult problem.

SUMMARY

1. The literature concerning the incidence of congenital diaphragmatic hernia and its management during the early hours of life is reviewed briefly.

2. Sixteen cases of congenital diaphragmatic hernia in the newborn are reported. Thirteen of the cases were diagnosed clinically and managed by operation. The diagnosis was made on postmortem examination in 3 cases.

3. The diagnostic triad of dyspnea, cyanosis, and "dextrocardia" was observed consistently in those infants in whom the diagnosis was made during the early hours of life. The frequent occurrence in these infants of the illusion of dextrocardia, secondary to the shift of the mediastinum into the right hemithorax, is emphasized.

4. All of the patients had left diaphragmatic hernias which were basically of the posterolateral, foramen of Bochdalek type. A hernia sac occurred in 3 of the 16 cases.

5. Seven of the infants were males and 9 were females. One infant was a negro and the remainder were white. Additional congenital malformations, other than the accompanying disturbances in midgut rotation and fixation, were encountered in 5 of the 16 patients.

6. All of the 13 patients who were managed by operation were treated during the first 90 hours of life, 11 of them being under 40 hours of age at the time of operation. All older infants were excluded from this study. An abdominal incision was employed in 11 cases and a thoracic incision in 2 cases. Eight infants recovered and 5 died.

7. In the great majority of cases, the ipsolateral lung was found at operation to be small, collapsed, and nonexpansible. No expansion of the left lung at the time of operation could be obtained in 8 of 11 cases. Expansibility was minimal in 2 cases and moderate in 1.

8. Although microscopic evidence of extensive atelectasis was found, the alveolar structure was observed to be mature in all cases available for postmortem study.

9. Unilateral hyaline membrane disease, involving the right lung, was found in 1 case. The collapsed and never expanded left lung was completely free of the pathologic changes characterizing hyaline membrane disease.

10. Postoperative roentgen studies suggest that, if the infant survives, slow but progressive expansion of the left lung may be expected. This observation was repeatedly made in cases in which the left lung at operation was observed to be small, collapsed, and nonexpansible.

11. Both the futility and the hazard of vigorous attempts to expand the small, collapsed, and nonexpansible left lung by positive pressure through an endotracheal tube at operation or by chest suction immediately following operation are emphasized.

12. The likelihood of not discovering the presence of a hernia sac in infants operated upon through an abdominal incision during the early hours of life is discussed. Presumably this failure to identify a sac, when present, results from its close approximation by the negative intrathoracic pressure to the

collapsed and nonexpansible lung. Closure of the hernia defect in the presence of an unrecognized sac creates a large cyst on the superior surface of the involved diaphragm. In order to avoid this complication when an abdominal incision is employed, the supplemental use either of a small intercostal thoracic incision or an incision in the pleura of the chest wall from inside to release the negative intrathoracic pressure and permit a sac, if present, to fall away from the nonexpansible lung is suggested.

13. The importance of the role of the obstetrician in establishing an early diagnosis is stressed. It is urged that immediate roentgenograms of the chest be made in the early minutes of life in all newborn infants who do not breathe easily and spontaneously after birth.

14. Early operation is recommended to provide an optimum climate for the slow and progressive expansion of the left lung and to avoid increasing pulmonary compression from the distention of intrathoracic gastric and intestinal viscera with swallowed air.

15. It is urged that the possibility of employing some means of artificial oxygenation of the blood to support these infants with nonexpansible lungs during operation, and perhaps the early hours of life, be investigated.

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AN APPRAISAL OF ONE STAGE ANTERIOR RESECTION IN DIVERTICULITIS OF THE SIGMOID COLON

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As IN SURGERY for other lesions of the large bowel, the surgical treatment of diverticulitis of the sigmoid and descending colon has undergone marked change in the past decade. As the rate of resectability has increased and operative mortality rates have decreased, there has been general acceptance of the need to remove the involved segment of bowel. Hence, a distinct trend away from multiple stage procedures toward one stage resection and primary anastomosis can be detected. Welch, Allen, and Donaldson, reviewing the records of 114 patients with diverticulitis treated by resection of the sigmoid in the Massachusetts General Hospital from 1942 to 1953, reported that 40 one stage resections with anastomoses were carried out, and that 57 per cent of the operations done in 1951 and 1952 were of this type. This is in sharp contrast to the report by Smithwick from the same hospital, for the years 1928 to 1942, during which only 6 one stage resections were carried out, in all of which cecostomy either was done concomitantly or had been done previously. Other observers have noted a similar change in their operative procedures.

Pemberton, Black, and Maino exhaustively reviewed the experience of the Mayo Clinic in the treatment of diverticulitis of the sigmoid colon over the years 1908 to 1945, inclusive. They were stimulated to do this by their observation of a change in surgical attitude after the routine use of sulfonamides for preparation of the bowel. Although they concluded that the safest plan of treatment is the establishment of a colonic stoma proximal to the lesion in association with an exteriorization type of procedure, they recognized the potentialities of broadening the indications for surgical treatment of diverticulitis and at the same time increasing the number of one stage resections with primary anastomoses in selected cases. In the years 1908 to 1944 only 17 of 384 (5 per cent) patients with diverticulitis operated upon at the Mayo Clinic were regarded as suitable for this procedure. Among these patients the operative mortality rate was found to be 12 per cent.

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NATURE OF PRESENT STUDY

In the past decade, coincident with the widespread use of antibiotic agents, both parenterally and as a method of sterilization of the bowel, the changes envisaged by Pemberton and associates have materialized. In view of the new trend encouraged by the clinical success of less conservative surgical procedures, the records of all patients who had diverticulitis of the sigmoid treated surgically at the Mayo Clinic between 1945 and 1954, inclusive, were studied. It was believed that data derived from such a study might be of value in reinforcing or rejecting presently held views and, perhaps, in formulating new concepts of therapy.

Currently, there are two main points of interest. The first concerns the possible desirability of offering elective resection to patients whose disease is relatively quiescent in order to forestall the development of serious complications. This differs markedly from the general attitude prior to 1945, when it was almost universally the practice to operate on patients with diverticulitis

TABLE I.—SURGICAL PROCEDURES PERFORMED FOR DIVERTICULITIS IN 320 CASES: 1945–1954

Procedure	*Patients*	*Per cent*	*Deaths*	*Per cent**
Anterior resection †				
1 stage	93	29.1	1	1.1
2 stage	47	14.7	2	4.2
3 stage	81	25.3	0	0
Obstructive resection †				
1 stage	53	16.6	3	5.7
2 stage	1	0.3	0	0
3 stage	16	5.0	0	0
Transverse colostomy only	22	6.9	4	18.2
Biopsy only	1	0.3	0	0
Diverticulectomy only	2	0.6	0	0
Miscellaneous	3	0.9	0	0
Drainage only	1	0.3	0	0
Total	320	100.0	10	3.1

*Per cent of patients undergoing the procedure.
†These terms are explained in the text.

TABLE II.—INCIDENCE ACCORDING TO AGE, 320 PATIENTS WITH DIVERTICULITIS TREATED SURGICALLY: 1945–1954

	All patients		*1 stage anterior resection*		
Age, yrs.	*No.*	*Per cent**	*No.*	*Per cent**	*Per cent of age group †*
20–29	2	0.6	0	0	0
30–39	12	3.8	2	2	17
40–49	60	18.8	19	20	32
50–59	114	35.6	34	37	30
60–69	99	30.9	28	30	28
70–79	31	9.7	9	10	29
80	2	0.6	1	1	50
Total	320	100.0	93	100	29
Mean age, yr.	56.8		56.8		
Range, yr.	26–81		30–81		

*Per cent of patients in series undergoing one stage anterior resection per decade.
†Per cent of total patients in each age group.

only when complications were already obvious. If the indications for operation are to be extended, it is essential to ascertain that the period of hospitalization and associated morbidity and mortality rates compare favorably with those obtaining when no operation is done.

The second point of interest concerns the possible application of one stage resection with primary anastomosis to a greater percentage of patients who come to operation, with consequent avoidance of the prolonged illness, multiple operations, and extended hospital stay that have attended the surgical treatment of diverticulitis in the past.

Three hundred twenty patients underwent operation for diverticulitis of the sigmoid between 1945 and 1954, inclusive. Of these, 93 (29.1 per cent) underwent one stage resection with primary anastomosis. The main purpose of this study was to appraise the clinical features and operative results in this group of 93 patients against the broad background of the remaining 227 patients for whom various different procedures were felt to be indicated. Consequently, attention has been focused chiefly on the group of 93 patients for whom primary resection was done, with end-to-end anastomosis but without associated colostomy. Two hundred twenty patients underwent multiple procedures (Table I). Eight of the 93 patients who underwent one stage operations had had some minor earlier operative treatment, such as incision of an abscess arising from the area of diverticulitis. In none of these had the subsequent one stage resection been appreciably facilitated by the previous intervention.

Definition of terms. The various procedures involved are listed in Table I in abbreviated form. The definition of those procedures is as follows.

Anterior resection:

1 stage: implies nonperformance of colostomy or cecostomy at any time.

2 stage: implies the establishment of a preliminary colonic stoma which is closed or removed at the time of removal of the segment of bowel affected by diverticulitis.

3 stage: implies the establishment of a preliminary colonic stoma which is subsequently closed by a separate operation after removal of the segment of bowel affected by diverticulitis.

Obstructive resection:

1 stage: implies removal of the segment of bowel affected by diverticulitis; a 3-bladed Rankin type clamp is employed, and subsequent spontaneous or surgical closure of the resulting fistula ensues.

2 stage: implies the establishment of a preliminary colonic or cecal stoma which is removed or closed at the time of resection.

3 stage: implies the establishment of a preliminary colonic stoma, subsequently closed at a separate operation after removal of the segment of bowel involved by diverticulitis, over a Rankin type clamp.

AGE AND SEX

The ratio of males to females in the total series of 320 was 1.6 to 1, which is in agree-

TABLE III.—FINDINGS IN ONE STAGE ANTERIOR RESECTION

	Operations	
	All	*1 stage*
Sex distribution	1.6 M:1 F	1.1 M:1 F
1945–1949	149	19 (13%)
1950–1954	171	74 (43%)
1954	35	20 (57%)
Operative findings at 1 stage procedure		
Fistulas:		19
Sigmoidovesical	15	
Sigmoidocutaneous	3	
Sigmoidovaginal	1	
Adherence:		44
Bladder	17	
Left adnexa	11	
Uterus	7	
Ileum	4	
Right adnexa	3	
Ant. abdominal wall	2	
Marked localized peritonitis		34
Length of bowel removed, average, cm.		16
Stay in hospital, average, days		16
For 6 patients more than, days		30

ment with the preponderance of males in other series, but the ratio of males to females was only 1.1 to 1 among the 93 who had undergone one stage resection. Part of this difference may be accounted for by the markedly decreased incidence of urinary complications in the female, in whom the uterus and adnexa frequently act as anatomic barriers, walling off the inflammatory process from the bladder. Furthermore, the contours of the female pelvis make low anastomosis an easier technical procedure than in the male.

In the total series of 320 patients, the ages ranged between 26 and 81 years, and among the 93 who underwent one stage resection, the range was from 30 to 81 years. The mean age in the two groups was identical: 56.8 years (Table II).

PREOPERATIVE FINDINGS: 93 PATIENTS WHO UNDERWENT ONE STAGE OPERATIONS

There were many and varied reasons influencing the initial decision to operate on patients in this group, but broadly, one or more of the following features dominated this decision.

Length of illness and repeated attacks. In view of the natural history of diverticulitis, with its tendency toward complete remission under adequate medical therapy, the first attack or subsequent episodes of mild difficulty were not regarded as sufficient reason for advising operation. More than half of these 93 patients complained of several moderate to severe bouts, often necessitating hospitalization elsewhere on at least one previous occasion. While the duration of the typical symptoms of diverticulitis ranged from 1 week to 11 years, 46 patients (50 per cent) had suffered from their disease for more than 6 months and 29 (31 per cent) for more than 2 years. In the half who were operated upon within 6 months, the decision was motivated by the presence of one or other of the complicating factors described below.

Recurrent fever with or without chills. Forty-six (50 per cent) patients recorded recurrent fever, with or without chills, as one of their major complaints. It is probable that this figure should be higher. Frequently, as the number of attacks of inflammation and accompanying pain increased, this feature became more prominent and disabling, and was associated in many cases with the symptoms of subacute colonic obstruction. Some patients undoubtedly had walled-off perforations, but the response to broad spectrum antibiotic agents usually was rapid.

Subacute colonic obstruction. It was difficult to arrive at the exact number of patients in whom subacute colonic obstruction had developed in the past. To judge by symptoms alone, more than half of the patients had on one or more occasions retired to bed with cramps, distention, borborygmus, and reduction or absence of flatus. In 4 cases, virtually complete obstruction persisted for a short time, probably caused by the congestion and edema of the inflammatory process in the narrowed bowel. All these difficulties resolved spontaneously, but several patients required hospitalization during the attacks.

Fistulas. Nineteen fistulas were present in 18 patients (Table III). Of these fistulas 15 were sigmoidovesical, 2 of which occurred in women, neither of whom had undergone hysterectomy. All fistulas were associated with pneumaturia, but only a few patients had noted fecal matter in the urine. Five of

the 15 patients (33 per cent) with sigmoidovesical fistulas had symptoms of diverticulitis for less than 6 months. The average duration of symptoms before the patients were seen here was 21 months. Recurrence of a fistula did not take place in any patient for whom the fistula was repaired during the course of a one stage procedure.

In addition to the 15 patients who had overt sigmoidovesical fistulas, 14 more complained of dysuria and frequence. In many of these, the sigmoid was firmly bound down by the inflammatory process to the bladder and, in some, development of a fistula obviously was impending.

Presence of a mass. In 44 cases (47 per cent) of the 93 a mass was palpable clinically. In 24 of these it was best felt in the left lower abdominal quadrant, but in 20 cases it was more easily palpable by rectal or vaginal examination. In some of the latter cases the preoperative diagnosis was thought to be carcinoma of the ovary, in view of the absence or paucity of intestinal symptoms. In a few, the possibility of carcinoma of the sigmoid which had prolapsed into the pelvis could not be excluded.

Melena. One patient was operated on primarily for rectal bleeding. A 49 year old woman had passed a fair amount of bright blood on 2 successive days about a week before admission. She felt perfectly well and had no other complaints. Sigmoidoscopic examination revealed sloughing, necrotic tissue suggestive of carcinoma, but the tissue removed from the bowel contained a large, benign ulcer only.

Eight of the 93 patients (9 per cent) had noted bright blood in the stool, but the quantity had not been excessive in any. Considered in conjunction with a recent loss of 33 pounds, this gave cause for concern in 1 patient but, at operation, uncomplicated diverticulitis was present.

Resemblance to carcinoma. The fact that in about 25 per cent of cases it may be difficult to distinguish diverticulitis from carcinoma has long been recognized, and in the absence of new diagnostic techniques, this difficulty persists. The presence of a mass in association with an equivocal roentgenologic report and unhelpful sigmoidoscopic findings was considered an absolute indication for operation.

Sigmoidoscopy was regarded as an integral part of the preoperative examination because of its value in excluding associated lesions. In those cases, however, in which there was complete obstruction to the flow of barium or in which the radiologist could not exclude the diagnosis of carcinoma with assurance, the bowel was so fixed, narrowed, and angulated that sigmoidoscopy was not helpful in distinguishing between these conditions. In other words, sigmoidoscopy tends to fail when help is most needed.

Thorough preoperative roentgenologic examination of the large bowel also is regarded as essential. In about 77 per cent of these 93 cases this procedure confirmed the diagnosis of diverticulitis. In many it outlined the degree and extent of involvement, but in 5 cases (5.4 per cent) the roentgenologic appearance was that of carcinoma; in an additional 5 cases the radiologist thought that the lesion probably was malignant. In the remainder of the cases the roentgenologic diagnosis was equivocal.

Miscellaneous. In 1 case, laparotomy had been performed elsewhere 10 days previously, and a diagnosis of carcinoma of the ovary had been made, but no definitive procedure was performed.

In 1 case, the inflamed sac of an incarcerated inguinal hernia was opened and the presence of pus containing Escherichia coli led to the discovery of acute perforating diverticulitis which was promptly and successfully treated surgically.

In the course of an operation for rectal prolapse, a third patient was found to have a mass caused by diverticulitis in the midpart of the sigmoid. The affected segment was removed.

TYPES OF OPERATIVE PROCEDURES: GENERAL ASPECTS

The number of patients with diverticulitis of the sigmoid operated upon annually has

TABLE IV.—NUMBER AND TYPE OF OPERATIVE PROCEDURES PERFORMED ANNUALLY

Year	Anterior resection			Obstructive resection			Transverse colostomy	Biopsy	Diverticulectomy	Miscellaneous	Drainage only	Total
	1 stage	2 stage	3 stage	1 stage	2 stage	3 stage						
1945	3	5	9	7	1	3	1	1	1	0	0	31
1946	2	1	5	11	0	3	3	0	0	0	0	25
1947	3	7	13	4	0	2	5	0	0	0	0	34
1948	3	5	5	5	0	1	1	0	0	3	0	23
1949	8	6	12	6	0	1	3	0	0	0	0	36
1950	12	5	11	2	0	2	0	0	0	0	0	32
1951	11	6	4	2	0	1	2	0	1	0	0	27
1952	14	3	8	5	0	2	6	0	0	0	0	38
1953	17	4	9	8	0	0	0	0	0	0	1	39
1954	20	5	5	3	0	1	1	0	0	0	0	35
Total	93	47	81	53	1	16	22	1	2	3	1	320

not shown any marked fluctuation or increase. Whereas between 1941 and 1945 about 24 per cent of all patients who received the diagnosis of diverticulitis at the Mayo Clinic were operated upon, this percentage for the period 1945 to 1954 was approximately 21. Of these, only 13 per cent underwent one stage resection in the years 1945 to 1949, compared with 43 per cent treated in that manner between 1950 and 1954 inclusive, and 57 per cent in 1954 alone.

This increase in the annual percentage of patients with diverticulitis thought suitable for one stage resection has been fairly steady (Fig. 1). It has occurred at the expense of all the other commonly employed procedures (Table IV). About 10 per cent of patients when first seen at the Mayo Clinic, however, already had undergone a previous operation (usually transverse colostomy) which automatically excluded them from the group in which one stage resection was done. In recent years, fewer such patients have presented themselves.

The rate of resectability has continued to increase, from 60 per cent between 1908 and 1940 and 77 per cent between 1941 and 1945 to 91 per cent between 1946 and 1954.

OPERATIVE FINDINGS IN 93 ONE STAGE RESECTIONS

In the years 1940 to 1944 only a single one stage resection, with primary anastomosis but without associated colostomy, was performed for diverticulitis of the sigmoid. When it was found that 93 such operations had been done during the next 10 years, the possibility that most of this change could be accounted for by a new willingness to operate for minimal diverticulitis was investigated. However, on the basis of operative findings alone, even without consideration of any associated clinical data that might suggest operation, this conclusion was discounted (Table III).

At the time of operation 18 patients had well established fistulas connecting with the sigmoid. Of these fistulas, 15 involved the bladder, 3 the skin, and 1 the vagina (1 patient had 2 fistulas, involving bladder and skin). Of the 15 sigmoidovesical fistulas, 2 developed in females, neither of whom previously had undergone hysterectomy.

In 44 cases there was well marked adherence to neighboring structures. In 17 this was maximal over the fundus of the bladder, but perforation had not yet occurred. In the great majority of these, after the inflamed bowel was disconnected, it was necessary to reinforce the wall of the bladder with a few sutures. In 21 cases there was marked adherence to the uterus or adnexa or to both. The frequent occurrence of associated left tubo-ovarian abscess and perforation on to the left tube and ovary was noteworthy. In such instances the left ovary and tube also were removed.

In 34 cases the affected loop was associated with severe localized peritonitis characterized by increased vascularity, edema, small mesocolic abscesses, numerous firm adhesions, and widespread woodiness that often made the initial dissection unusually difficult, especially over the region of the

left ureter. Once the procedure had been carried beyond the confines of the area of maximal inflammation, however, the bowel above and below the proposed line of anastomosis could be sufficiently mobilized in all cases to avoid undesirable tension.

The average length of bowel removed was 16 centimeters, as measured in the laboratory. There was no significant difference between this and the length of the segment removed in multiple stage procedures. It was not considered necessary to remove all diverticula beyond the area of inflammatory involvement where this might cause tension on the anastomosis. No patient appeared to suffer any complications from residual noninflamed diverticula. When it was noted in preoperative roentgenograms made with the aid of a barium enema that many diverticula were present throughout the descending colon, the involved area was removed, and transverse colosigmoidostomy was performed.

Despite the fact that many of these patients had suffered numerous and often recent episodes of subacute obstruction, undue dilatation of the bowel proximal to the lesion did not present itself as a technical problem. On the other hand, the lumen of the distal portion of bowel, especially when the upper part of the rectum was employed, sometimes appeared uncomfortably narrow.

TABLE V.—18 COMPLICATIONS OF 93 CONSECUTIVE ONE STAGE ANTERIOR RESECTIONS

Complication	*No.*	*Comment*
Hematemesis from duodenal ulcer	1	Death
Cerebrovascular accident	1	Progressive recovery on dismissal
Intestinal obstruction due to adhesions	1	Reoperation twelfth postoperative day; transverse colostomy
Partial dehiscence	2	Associated obstruction in 1 patient; associated wound infection in 1
Anastomotic abscess with stenosis	1	Transverse colostomy after operation. Re-resection later
Wound infection	5	Mild in 4 patients; 1 required 42 days in hospital
Fecal fistula	5	Four patients resolved spontaneously; 1 required transverse colostomy
Transurethral resection	2	Males, aged 57 and 69 yrs., with prostatism
Total	18*	

*16 patients had 18 complications.

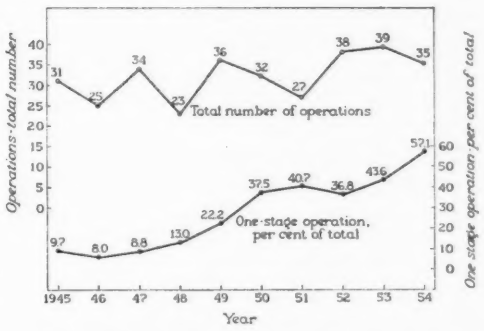

FIG. 1. The increase, between 1945 and 1954, in the number of patients with diverticulitis who have been thought suitable for one stage resection.

Despite this, apart from a single case (Table V), no complication associated with stenosis of the anastomotic line was encountered. About 40 per cent of the anastomoses were done aseptically, with the use of a Rankin three-bladed clamp.

The difficulty of distinguishing diverticulitis from carcinoma, even with the involved segment of bowel at hand for gross inspection, has long been noted. This difficulty was encountered in 20 of the 93 cases (21 per cent) and led to extensive dissection in all cases in which doubt remained after careful examination.

MORBIDITY AND MORTALITY RATES

There were 18 complications in 16 patients among the 93 patients who underwent one stage resection (Table V). Of these, 6 complications were related to the anastomosis. In the single case in which stenosis at the anastomotic line developed, the one stage resection had been done after a fistulous tract leading from the midsigmoid to the pararectal area had been dissected and removed. An abscess formed at the line of anastomosis, necessitating performance of defunctioning transverse colostomy on the twelfth postoperative day. By the time the patient returned for consideration of closure of the colonic stoma 6 months later, the stenosis had become established. It required re-resection and anastomosis for relief.

Among the 5 patients in whom fecal fistulas developed the fistulas formed between the sixth and tenth postoperative days. Four closed spontaneously, 3 within a few weeks, and 1 after 5 months. The fifth patient required temporary transverse colostomy.

Two men, aged 57 and 67 years, noted to have prostatism preoperatively, subsequently required transurethral resection. In both cases, unusually extensive dissection, with sigmoidorectostomy, was necessary. In the first of these 2 patients, it had not been possible to distinguish between diverticulitis and carcinoma at operation, and in the other, widespread inflammation was associated with a sigmoidovesical fistula.

There were 4 mild infections of wounds which did not appreciably lengthen the patients' hospital stay, and 1 more serious infection which required treatment in the hospital for 42 days.

Partial dehiscence took place in 2 cases, associated with obstruction and excessive distention in one, and the presence of an abscess in the other.

One patient sustained a severe cerebrovascular accident on the first postoperative day, but made steady progress and was much improved when dismissed on the thirty-third postoperative day.

There was only 1 death among the 93 patients (1.1 per cent). This occurred in a 70 year old man on the sixteenth postoperative day after exsanguinating hematemesis. At necropsy a bleeding duodenal ulcer was found.

The average hospital stay of patients who underwent one stage resection was 16 days. Only 6 patients, because of complications, were required to remain in the hospital longer than 30 days. This factor is obviously of great importance to the patient, mentally, physically, and economically, and it must be contrasted with the complications, and morbidity and mortality rates accompanying multiple stage procedures, the effect of successive periods of hospitalization on morale, and the many undesirable features of a temporary colonic stoma.

There were 9 deaths (4.1 per cent) among the 220 patients for whom multiple stage operations were performed in the same period, a very much greater rate for complication than that among the patients who underwent one stage procedures (Table VI). The increased morbidity and mortality rates in the former group were anticipated, because most of the emergency admissions and many of the patients with more acute diverticulitis were included in this group. Nevertheless, it should be emphasized that a large number of the patients who underwent one stage resection presented more acute and extensive disease at the time of operation than did many for whom a multiple stage procedure was carried out. Naturally, the decision as to the most desirable type of procedure varied among individual surgeons, but the trend away from multiple stage operations in the more recent years of the study has been striking. This has not been attended by increasing morbidity rates.

COMMENT

In view of continuing advances, it is necessary to re-evaluate regularly the general policies of treatment which are applied to individual conditions. Too often, treatment can be unduly influenced and hampered by outmoded concepts. It is increasingly evident that the attack on diverticulitis of the sigmoid may, with justification, be conducted today in a far more radical manner than before. The evolution of this attitude over the past 20 years has been gradual, but it has increased in tempo in recent years.

In the mid-thirties the surgical treatment of diverticulitis was attended by very high morbidity rates and excessive mortality risks. This was not unique, for other operations necessitating extensive resection of the colon also were accompanied by great risk. The hazards involved in diverticulitis were, however, further increased by the accepted practice in those years of awaiting the development of complications before operation was advised. Unfortunately, this attitude has not yet disappeared.

Since 1950, partly as a result of the effectiveness of available antibiotic agents in preparation of the inflamed bowel, there has been increasing acceptance of one stage resection, with primary anastomosis but without colostomy, in selected cases. In view of this, there is need of reappraisal of the criteria which influence the decision as to operation. On the one hand, unnecessary operations must be avoided, and, on the other, operation must bring benefit without unwarranted morbidity or mortality.

The primary treatment of uncomplicated diverticulitis remains medical. Now that many broad spectrum antibiotic agents are available, many attacks of the disease can be abated rapidly, while others may be more gradually controlled. Operation may then be undertaken under more favorable conditions, if the suitable indications are present. A major concern is that of attempting to ascertain the group of patients who will continue to have recurrent incapacitating attacks leading ultimately to dangerous complications and long term illness. Ideally, recognition of this group should take place at a time when resection can be performed as a one stage procedure. The main premonitory signs shaping the decision as to early resection for a patient otherwise well are (1) recurring attacks of abdominal pain and fever, despite good medical management, (2) episodes suggestive of subacute obstruction, (3) evidence of one or more subacute perforations with localized peritonitis, (4) the association of more than minor urinary symptoms, (5) the presence of a mass that does not resolve with reasonable rapidity after antibiotic therapy, and (6) lower intestinal bleeding in the presence of diverticula of the sigmoid, after other lesions that might be responsible have been excluded.

There is no question that the multiple stage operation will continue to occupy a prominent place in any selection of operations for diverticulitis. Defunctioning colostomy may be lifesaving in an emergency, and should always be carried out as a safety measure when doubt exists as to the lasting qualities of any anastomosis. Conversely, in the modern era of surgery, the defunctioning colostomy should not be regarded as a routine concomitant of resection. Certain postoperative complications and even the possibility of death inherent in the establishment of a colonic stoma naturally are avoided in the performance of one stage resection. Furthermore, the colonic stoma, in the absence of resection of the diseased area of bowel, does not necessarily produce clinical improvement.

TABLE VI.—COMPLICATIONS IN 220 CONSECUTIVE MULTIPLE STAGE PROCEDURES*

	Cause	*No.*
Deaths, 9 (4.1 per cent)	Peritonitis	3
	Pulmonary embolus	2
	Pseudomenbranous enterocolitis	2
	Atelectasis	1
	Cerebrovascular accident	1
Other complications	Those of the colonic stoma	
	Wound infections	
	Intestinal obstruction	
	Adhesions	
	Incarceration in lateral gutter	
	Anastomotic stenosis	
	Continuing or recurrent inflammation in sigmoid	

*Includes cases in which a colonic stoma was established with no subsequent procedure.

It is of some interest that most of the one stage resections done in the early years of this series were prompted by the inability of the surgeon to distinguish definitely between carcinoma and diverticulitis, or for some other unusual reason. The patients concerned had uncomplicated courses, a fact which encouraged the gradual extension of this operation to other patients in whom the inflammatory process unquestionably was caused by diverticulitis.

It thus became apparent that adequate one stage resection can be performed with an impressively negligible mortality rate. In our series of 93 consecutive one stage resections, the only death which occurred was unrelated to the operation. Complications were not many, and few were serious. The vast majority of these patients were spared long periods of hospitalization and the associated economic loss. While it is obvious that the results were obtained in a selected group,

no patient who had minimal diverticulitis underwent resection. The fact that 15 sigmoidovesical fistulas were included in the removed specimens without complication seems to invalidate the widely held view that such fistulas unequivocally must be dealt with by multiple stage operations.

We believe that the one stage operation has an increasingly prominent place among the surgical procedures designed for diverticulitis of the sigmoid. Although it never can completely supplant multiple stage operations, the one stage procedure can greatly reduce the need for these if patients who eventually will require operation are recognized earlier, and if the surgeon, at the time of operation, will not indiscriminately apply some set method of treatment. At present, it is probable that 80 to 90 per cent of patients with diverticulitis could undergo one stage resection with the promise of excellent results.

SUMMARY AND CONCLUSIONS

There has been a noticeable trend in recent years toward the more frequent application of one stage resection, with primary anastomosis but without colostomy, in diverticulitis of the sigmoid colon. Antibiotic therapy has been largely responsible for this fact by aiding resolution of the inflammatory process in the acute phase, and consequently making elective surgery, with a reduced mortality rate, possible. Of the 320 operations performed for this condition at the Mayo Clinic between 1945 and 1954, 93 (29 per cent) were done in this manner. The mortality rate was 1.1 per cent. During these years, the rate of resectability was 91 per cent, an appreciable increase over that of earlier series.

At the same time, there has been a steady increase in the percentage of patients regarded as suitable for this type of operation. This is only in part attributable to a deliberate effort to advise elective resection before the onset of complications has made a single stage operation unfeasible. A plea for earlier recognition of those patients who subsequently will require operation is made. Advances in colonic surgery justify a less conservative attitude than has heretofore prevailed. The other factor accounting for this increase in one stage resections has been the recognition that this procedure can be performed safely in certain cases in which there is persistent inflammation and established fistulas, provided sound judgment is employed. The old rigid criteria, which decreed that the presence of obstruction of even minor degree or fistula, or localized active peritonitis, automatically demands a preliminary defunctioning colostomy, are no longer tenable. In each case the situation should be judged by the living pathologic process that is exhibited at the time of laparotomy.

The primary treatment of diverticulitis remains medical. About 80 per cent of the patients will respond satisfactorily. The rest will require resection of the affected segment of bowel. For those who require operation urgently or in whom the inflammatory process is unduly acute or extensive, the desirability of a multiple stage operation remains unchallenged. It is among the remainder that the one stage operation has been shown to be applicable, in the majority of cases, with the promise of most satisfactory results. In this series of 93 consecutive cases in which one stage resection was performed in this manner, postoperative difficulties were few, the hospital stay averaged 16 days, there have been no known recurrences, and the single death which occurred was unrelated to the operation.

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THE HELIX RESERVOIR PUMP-OXYGENATOR

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FOR TWO YEARS at this institution total body perfusion (3, 5, 10) by means of a pump-oxygenator has been regularly utilized in man to permit open intracardiac surgery at normal temperatures. This apparatus has proved itself dependable and safe in routine clinical application in over 250 patients. The following presentation describes the experimental data leading to the successful development and clinical application of this simple and effective artificial oxygenator.

METHODS OF STUDY

Apparatus. Figure 1 represents the oxygenator which ultimately developed as a result of these studies. It is a large bubble oxygenator composed of five essential elements: mixing column, debubbling chamber, helix reservoir, arterial filters, and the cardiotomy aspiration chamber. In the blood oxygen mixing column oxygenation of the blood occurs at the blood gas interface of the large bubbles simultaneously with the diffusion of the excess carbon dioxide out of the blood. The bubble formation in this oxygenator is a gentle process in which the venous blood is filmed upon the surface of the oxygen globule without foam formation. The debubbling chamber is coated with a potent nontoxic silicone preparation which facilitates the release of excess oxygen and carbon dioxide from the chamber by dissipating the bubbles and allowing the blood to flow smoothly into the helix reservoir. This reservoir effectively removes any remaining minute bubbles and insures the safety of the artificially oxygenated blood. The entire helix reservoir is immersed in a constant temperature water bath for maintenance of the patient's normal body temperature during the perfusion. A filter is placed on the afferent (aspiration) limb of the arterial pump rather than the efferent (pressure) limb. The afferent limb is preferred since the potential force seeking to drive any particulate matter through the filter is substantially less than the force that may develop on the efferent side of the Sigmamotor pump.

Blood entering the heart from the coronary sinus, thebesians or bronchials during the by-pass is aspirated by means of a low vacuum suction tip and collected in a chamber positioned below the oxygenator. This blood is then returned to the blood oxygen mixing column by a separate pump.

A multiple finger, cam actuated pump was used as the blood propelling mechanism in these experiments.

EXPERIMENTAL PROCEDURE

Seventy mongrel dogs varying in weight from 4.5 to 49 kilograms were studied by utilizing a series of biochemical determinations to be indicated, before, during, and after the total body perfusions.

Each animal was premedicated with approximately 1.5 milligrams of morphine sulfate per kilogram body weight, in addition to a routine dose of 0.6 milligram of atropine sulfate administered about 1 hour preoperatively. Anesthesia levels were maintained with 2.5 per cent intravenous sodium pentothal given in small increments throughout the procedure.

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During the open thoracotomy prior to and after the total by-pass interval these animals were respired with air by means of an endotracheal tube attached to a mechanical respirator. The right thorax of each animal was shaved and scrubbed with tincture of zephiran. All equipment used including the oxygenator was sterilized by autoclaving or boiling prior to each experiment.

The incision was made through the bed of the right fifth rib. Two umbilical tapes were placed around the venae cavae at their entrance into the right atrium so that they would exclude the entire venous return to the heart when they were tightened by drawing the ends of the tape through rubber cuffs and cross clamping the latter. A catheter was placed through the superficial jugular vein in the neck and positioned in the inferior vena cava. In addition, holes were placed in the shaft of this catheter so that the superior vena cava would be drained when the tapes were tightened to effect total cardiac inflow stasis. The arterial catheter was placed a short distance into either carotid artery. No preference was given as to which cava was opened or closed first at the onset or termination of the perfusion.

A series of biochemical observations, detailed later, were made in all 70 experiments during total cardiopulmonary by-pass, and 20 of these animals were in addition subjected to a right ventriculotomy. In survey experiments we have not been able to detect any advantages utilizing varying mixtures of oxygen and carbon dioxide for oxygenation; therefore, these metabolic studies were made using 100 per cent oxygen within the oxygenator.

The arterial blood used to prime the oxygenator reservoir was obtained from a donor dog's femoral artery by using anectine and procaine local anesthesia[1] while the animal was being hyperventilated by a mechanical respirator.

Blood clotting was supressed by 1.5 milligrams of heparin per kilogram body weight given intravenously to the patient animal just prior to the cannulations. The heparin effect was reversed by a similar amount of protamine sulfate given as a single dose at the conclusion of the by-pass. Heparin-protamine titrations were not found necessary. Chest catheters were placed in the posterior thorax of the animal prior to closing the thoracotomy incision and were removed several hours later when the pleural cavity was dry and the lungs well expanded. No blood transfusion was given to any of the animals during the postoperative period, but the animals received antibiotics for 5 days.

Conditions of the perfusion. All of these animals were perfused at rates less than their estimated total cardiac output, the quantities based on azygos flow studies (1, 2) and clinical experience with controlled cross circulation (8, 9). The perfusion rates employed varied from 16 to 50 cubic centimeters of blood per kilogram body weight per minute as part of a study to determine an optimum rate of flow as judged by the metabolic data. The pump was calibrated to deliver the desired minute volume of blood selected for the experiment, and this predetermined flow rate was maintained unchanged throughout the total by-pass interval. Comparative studies on perfusion rates between 50 and 100 cubic centimeters per kilogram per minute are now in progress.

The importance of maintaining the animal's body temperature stable was not well appreciated during the earlier experiments and as a consequence the rectal temperature of these animals fell to an average of 35 degrees C. by the end of the perfusion. In the later animals a normothermic status was maintained by immersing the oxygenator reservoir in a thermostatically regulated water bath.

Acid-base balance. To determine the degree of acid-base shift that developed during the perfusion, the total plasma bicarbonate concentrations corrected to a *p*H of 7.4 of the animal's blood was calculated by use of the

[1]The use of pentobarbital sodium (nembutal) or other long acting anesthesia for this purpose may cause death of the patient animal from anesthetic overdose.

Peters and Van Slyke formula[2] immediately prior to and after 20 minutes of total body perfusion. The differences between the control and final bicarbonate concentrations corrected to *p*H 7.4 represented the change in fixed acids in the plasma. This change of the plasma bicarbonate was calculated for each animal's perfusion, and the mean value of this alteration determined for each flow rate group.

Oxygen consumption rates. The oxygen consumption rates of the animals during the perfusion were calculated from the measured oxygen arterial venous difference, the constant perfusion rate, and the weight of the animals.

RESULT

Objective responses of the animals. An animal was considered to have tolerated the perfusion well if he awakened within 5 hours after the perfusion and was without any evidence of neurologic injury at that time or at any subsequent time. Forty-eight animals were considered by these criteria to have undergone the total by-pass interval unharmed. Ten animals were detectably injured by the procedure, but recovered within 1 to 5 days, after which time they appeared normal. Twelve animals died or were sacrificed within the first 3 days following the by-pass and all 12 were obviously injured as a result of the experiment. We have not observed any animals make an apparent recovery, to die at any time later of "unknown causes." In all cases of injury or death of the animal we were able to determine the reason for the failure and to remedy this error in design of the apparatus or in technique during subsequent studies. Thus, the design of the perfusion apparatus and technique of the perfusion varied considerably in the earlier experiments, but became standardized as experience and knowledge increased.

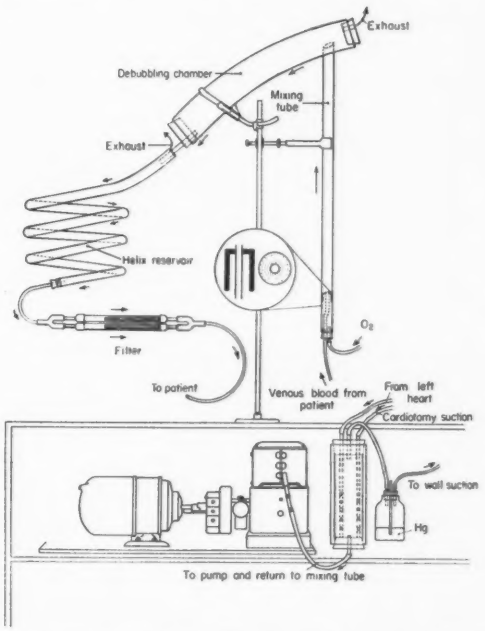

FIG. 1. Helix reservoir oxygenator. This apparatus has five essential components: blood oxygen mixing tube, debubbling tube, helix reservoir, filter, and cardiotomy blood reservoir system (shown on the lower level) with its own pump to return the blood directly to the afferent limb of the oxygenator. For many clinical procedures it is advisable to collect blood from a left heart vent in addition to the cardiotomy suction. The mercury trap on the wall suction limits the negative pressure to 30 to 50 millimeters of mercury to prevent traumatic blood damage.

Causes of failure. A careful inquiry into each of these perfusion failures was a most important factor leading to the successful evolution of this simple and effective oxygenator suitable for clinical use. Perfusions in 22 animals were considered failures. The mechanisms of failure were defined in each of these experiments, and in some instances were deliberately repeated several times for confirmation. For example, to test the usefulness of the helix reservoir, 9 experiments were conducted excluding the helix from the system and substitution of a vertical column of the same blood capacity as the helix. All

[2] $[HCO_3]\ pH\ 7.4 = [HCO_3]\ pH_x - [(7.4\text{-}pH_x)\ (8.2 + 2.3\ \text{hgb.})]$

Where:

$[HCO_3]\ pH\ 7.4$ = Total bicarbonate in the sample at *p*H 7.4.

pH_x = Animal's measured arterial blood *p*H.

$[HCO_3]\ pH_x$ = Total bicarbonate at pH_x obtained from nomogram from patient's known pH_x and total CO_2 content.

$(8.2 + 2.3\ \text{hgb.})$ = The slope of the buffer curve of whole blood with hemoglobin expressed as millimoles per liter which is $\frac{\text{hgb. in gms. per cent}}{1.67}$

TABLE I.—ACID-BASE CHANGES DURING TOTAL BODY PERFUSION IN DOGS RECEIVING DIFFERENT PERFUSION RATES

		Carotid artery					*Vena cava*					
Perfusion rate, c.c./kgm./min.	*No. of exper.*	*O_2 vol., per cent*	*O_2 sat., per cent*	*Total CO_2, mM./l.*	*CO_2 tension, mm.Hg*	*pH*	*Hgb., gms. per cent*	*O_2 vol., per cent*	*O_2 sat., per cent*	*Total CO_2, mM./l.*	*CO_2 tension, mm.Hg*	*pH*
Control*	63	17.1	98	18.2	22	7.53	13.0	11	63	22.0	30	7.48
16–20	4	17.5	99	13.3	30	7.26	13.1	2.6	15	20.3	65	7.10
20.1–25	9	12.2	100	14.0	29	7.30	13.4	3.9	22	19.2	51	7.18
25.1–30	12	12.1	100	14.4	26	7.36	12.7	4.6	28	19.5	44	7.25
30.1–35	12	19.2	100	17.0	32	7.34	13.9	6.3	34	20.1	46	7.25
35.1–40	11	20.0	100	17.2	30	7.36	14.2	7.0	37	22.5	48	7.27
40.1–45	7	18.1	100	15.4	26	7.38	13.0	8.5	49	20.6	42	7.30
45.1–50	7	19.3	97	18.0	32	7.36	14.7	10.6	54	21.1	48	7.27

*Mean values of all animals immediately before perfusion. Remainder of the values were taken after 20 minutes of perfusion with heart-lung by-pass still in progress.

circumstances of each of these perfusions were identical except for the exchange of a vertical reservoir in place of the helix reservoir. In these 9 experiments utilizing a vertical reservoir, 2 animals died, 6 were injured, and 1 was uninjured. The 8 damaged animals all showed signs of central nervous system injury. Six of these animals recovered from 1 to 5 days after the perfusion and appeared normal, the other 2 died within 24 hours. The 6 surviving injured animals and the 1 uninjured were probably protected by a bubble trap which had been placed at the outlet of the vertical reservoir to search for free gas in the arterial limb blood. A similar bubble trap used in conjunction with a helix reservoir routinely failed to show the presence of any bubbles in the arterial blood returning to the animal. Thus, the helix reservoir became an integral part of the oxygenator design.

Six animals died as a result of technical difficulties such as faulty mechanical respiration, errors in blood sampling (hypovolemia), and errors in operation of the oxygenator (early designs and inexperience).

TABLE II.—PLASMA BICARBONATE DEPRESSION AS A RESULT OF PERFUSION

Perfusion rate, c.c./kgm./min.	*Bicarbonate* deficit after perfusion, mM./l.*	*Mean wts. of animals in kgms.*
16–20	13.9	10.6
20.1–25	11.3	13.9
25.1–30	9.1	14.7
30.1–35	5.3	21.7
35.1–40	8.1	20.9
40.1–45	9.0	20.3
45.1–50	6.9	22.0

*Mean values of each group.

One 4.5 kilogram animal developed profound hypothermia during the perfusion and died of irreversible ventricular fibrillation shortly after the perfusion.

Finally, most important causes of failures were faulty application of the blood filters, or poorly designed catheter connectors. Blood passing a constricting area in a conduit at the higher perfusion rates will deposit friable clots of fibrin in dead spaces of poorly designed connectors which then may pass to the animal as emboli. Figure 2A demonstrates this danger. Increasing the degree of heparinization will not prevent this clot formation, but this complication may be avoided completely by properly designed conduit connectors as illustrated in Figure 2B. The lumen of the tubing is unobstructed by the connector and flow is streamlined. The same clot formation was observed at times, in the filters which we were using for these experiments. At the higher perfusion rates, clots would form about the constriction at one end of the filter. If the blood flow was in the direction of Figure 2D the clots would pass to the patient; however, if the blood flow was in the other direction as in Figure 2C the filter would trap these clots. This clot formation was eliminated by having the blood flow in the direction indicated by Figure 2C and by using several of these filters in parallel thus reducing the minute volume through each for added safety.

In another group of animals we utilized as an arterial filter, a long sock-like fine mesh tube of nylon, closed at its distal end and suspended by means of a specially de-

signed collar within the helix tubing near its exit end. Despite the apparent excellence, in theory, of the design of this filter, it proved lethal to most of the animals because the whipping action of this supple nylon tube within the pulsatile flowing stream of blood effectively defibrinated the blood producing a characteristic syndrome (abnormal hemorrhage due to loss of fibrinogen, and neurologic sequelae due to the emboli of fibrin).

In our consultations with others this "defibrination syndrome" due to poorly designed connectors, filters, and bubble traps interposed within the extracorporeal blood circuit has been the single most important cause of perfusion failures. These factors are independent of the type of extracorporeal oxygenator utilized. An observation aiding in the recognition of this complication is the fact that a short perfusion at a lower flow may appear entirely safe while a longer perfusion interval especially with a higher flow and thereby greater turbulence will result in failure of the animal (or patient) to awaken promptly, or at all, often combined with an unusual hemorrhagic tendency.

Some have confused this "defibrination syndrome" with sequelae due to air embolism, reactions to heparin, or to protamine "breakaway." It is also worthy of emphasis that blood defibrination is independent of hemolysis, and is not associated, as a rule, with high levels of plasma hemoglobin.

Acid-base changes. Tables I and II illustrate the acid-base responses of these animals to their perfusions. The control blood samples were taken directly from the indicated vessels immediately before the onset of the perfusion and therefore represent the combined effects of the anesthesia, artificial respiration, and thoracotomy prior to the actual heart-lung by-pass. It may be noted that a respiratory alkalosis was present in all of these animals prior to the start of their perfusions as reflected by their high arterial p_H values and lowered carbon dioxide tensions. The final samples were taken from the respective catheters after 20 minutes of total cardiopulmonary by-pass and with the perfusion still in progress. Thus, these values represent the blood going to and from the animals immediately before the termination of the perfusion. No base was administered to these animals before, during, or after the perfusion.

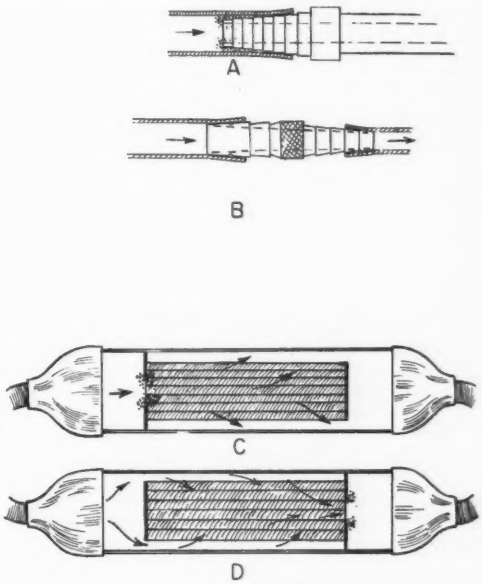

FIG. 2. Mechanism of clot formation by faulty blood conduits. At higher perfusion rates improperly designed blood conduits may cause clot formation in dead spaces and areas of turbulence formation. This can be eliminated by eliminating these dead spaces as in B. In case of the filter, several can be used in parallel thus providing a decreased flow through each which is below the flow rate necessary to cause clot formation. Blood flow as indicated in C safely traps any of these clots.

Table II is a quantitative comparison of the plasma bicarbonate alterations developed during the perfusion at the various perfusion rates. In general, it may be seen from this table that the lowest perfusion rates are associated with the greatest degree of plasma bicarbonate depression with a lesser depression occurring as the perfusion rate increases. However, another factor, the size of the animal, seems to have some relationship to these changes. Table II shows the mean weights of the animals in each perfusion group. The variations of the individual animal size with the perfusion rate and the amount of plasma bi-

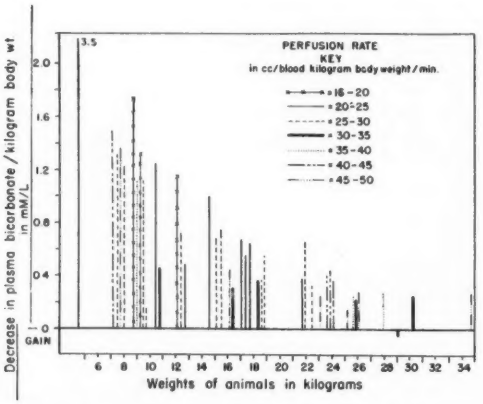

FIG. 3. Comparison between the perfusion rates, weight of the animals, and decrease in the plasma bicarbonate over a total body perfusion interval. The alterations in the plasma bicarbonate as a result of total body perfusion are related to the size of the animal and to the actual perfusion rates as well as the duration of the by-pass intervals.

carbonate depression per kilogram body weight in each experiment is plotted in Figure 3. This diagram indicates that the amount of plasma bicarbonate depression is greater in the smaller animals than in the larger at a given perfusion rate. Thus, the change in plasma bicarbonate was related to the animal's size and the perfusion rate.

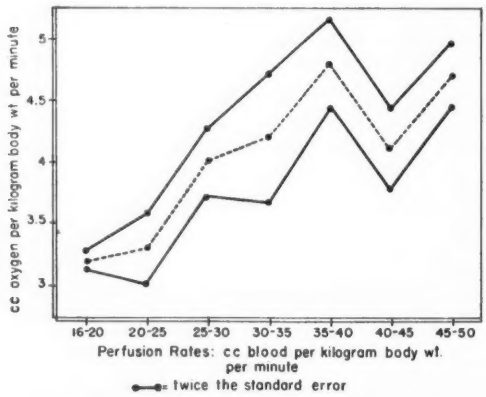

FIG. 4. Oxygen consumption rates during total body perfusion. Oxygen consumption rates during total body perfusions between 25 and 50 cubic centimeters per kilogram per minute were essentially the same and were higher than with perfusion rates less than 25 cubic centimeters per kilogram per minute.

As noted the arterial *p*H values were higher than normal at the beginning of the perfusion of the animals, and fell to their lowest point in the animals receiving the lowest blood perfusion rates which were also the smallest animals. With perfusion rates above 25 cubic centimeters per kilogram per minute, the arterial *p*H values at the end of the perfusion were between 7.34 and 7.38 (Table I).

Carbon dioxide was removed most efficiently by the oxygenator from the venous blood during the oxygenation process. The observed carbon dioxide levels were below the normal carbon dioxide content given for dog arterial plasma which is about 21.6 millimols per liter. The venous blood leaving the animal during the by-pass had normal (22.9 to 25.9 mM./l.) or slightly lower than normal carbon dioxide values. The normal arteriovenous carbon dioxide difference is about 3 millimols per liter. It is therefore apparent that the blood of these animals receiving reduced output perfusions return a larger amount of carbon dioxide per unit volume of blood to the respiratory apparatus than does blood during the normal state.

Oxygen content. The venous oxygen saturation as indicated in Table I is directly related to the perfusion rate. The venous blood returned to the oxygenator in all of these experiments was arterialized to a mean value of 99 per cent saturation.

Oxygen consumption rates. The oxygen consumption rates were calculated from the animal's blood samples taken just before the termination of the perfusion. These data are contained in Figure 4. These values for oxygen use varied from a low of 2.4 cubic centimeters oxygen per kilogram per minute to 6.4 cubic centimeters of oxygen per kilogram per minute. The oxygen consumption rates did not change significantly in perfusions above 25 cubic centimeters per kilogram per minute as indicated by the standard error calculations. Figure 5 compares the oxygen consumption rates with the perfusion rates and sizes of each animal. Within each perfusion group the smallest animal is charted to the left of the next heavier. Previously re-

ported values in humans (3) suggested that the smaller and younger the individual, the greater his oxygen consumption rate would be; however, this relationship was not apparent in these animal experiments.

Blood constitutients. The effects of the perfusions upon red cell fragilities measured by hemolysis in varying concentrations of saline were determined in 4 experiments. Control samples were compared with samples taken from the animal at the completion of the experiment. The tests were observed for a 48 hour period. In none of these samples was there any detectable difference in red cell fragilities between the control and the final samples. Hemolysis began at a saline concentration of 540 milligrams per cent and was complete at 450 milligrams per cent.

Unhumidified 100 per cent oxygen was used in the oxygenator for most of the experiments; therefore some dehydration of the blood might be anticipated. For this reason hematocrit determinations were measured in 6 experiments, but we were unable to demonstrate any significant differences between the control and the final samples.

Serial platelet counts, leucocyte counts, lactic acid and *p*H determinations were investigated in the first 22 experiments. All of these animals were run in the lower perfusion ranges. These data are presented in Table III and indicate a return to normal values within 2 hours after the perfusion.

Plasma hemoglobin values varied from 10 to 200 milligrams per cent in samples taken from the vena cava of the animal at the termination of the perfusion. The mean value for all of the experiments was 80 milligrams per cent plasma hemoglobin.

Blood loss in the postoperative interval varied from 30 to 300 cubic centimeters from the thoraces of these animals, but in no case was this loss replaced. It was our desire to determine if the animal would tolerate the procedure without even the usual postoperative assistance. In no case after completion of the preliminary survey studies already mentioned was the experiment a failure because of a hemorrhagic diathesis.

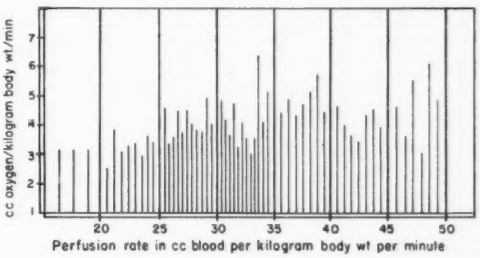

FIG. 5. Oxygen consumption rates comparing animal size with the perfusion rates. Within each perfusion group the smaller animal is placed to the left of the next heavier one. It could be expected that the smaller animals would have higher oxygen consumption rates as was true in humans; however, this assumption was not apparent in this study, no doubt because the smaller animals were not necessarily younger.

Systemic pressures during the perfusion. In 10 experiments arterial pressures were monitored at the bifurcation of the animal's aorta by means of a mercury manometer. Figure 6 represents these pressures during the experiment and illustrates the characteristic bradycardia observed during the by-pass.

DISCUSSION

The desirability of heat sterilization for blood oxygenator equipment is obvious. This apparatus is primarily constructed of a pure polyvinyl plastic which is readily autoclaved as are the remainder of the parts employed in its construction. In fact, it should be generally recognized that any pump-

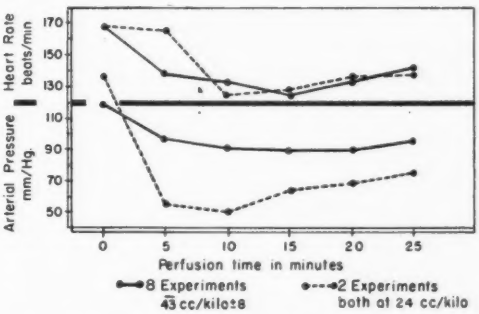

FIG. 6. Systemic pressures and heart rates during reduced volume total body perfusion. Perfusion rates above 40 cubic centimeters per kilogram per minute routinely maintained the animal's systemic pressure above 90 millimeters of mercury.

oxygenator system that cannot be heat sterilized will be unsafe for repeated clinical usage.

The other advantages of a bubble oxygenator, in addition to its simplicity and ease of construction, are in its efficiency in performing the respiratory functions. The oxygen content of the blood is rapidly raised to saturated levels regardless of its degree of desaturation before oxygenation, and the carbon dioxide of the venous blood is readily removed from the blood to normal or subnormal levels. The safety of its operation is demonstrated by these animal experiments and subsequent use in humans who have undergone total body perfusions during repair of intracardiac defects for periods up to 90 minutes and survived to be cured of their disease process (4).

Use of unsiliconized glass has been avoided by us in construction of the described perfusion apparatus as strong evidence was available that glass is a poor material to use in contact with blood if one wished maximally to preserve the clotting mechanism. The dangers of glass in a perfusion system are illustrated by the fact that studies of the coagulation process in glass containers are subject to considerable error. Glass has been demonstrated to activate many of the blood clotting precursors and to absorb thrombin from the blood. Glass surfaces are also well known for their ability to destroy platelets. Because of the adverse effects of unsiliconized glass on the blood clotting mechanism, we have preferred to avoid its use.

The helix reservoir has proved itself to be a major factor in the dependable and reproductible success of this bubble oxygenator. Two synergistic factors are the primary physical mechanisms which make this debubbling system work with wide margins of safety. These two factors are hydrostatic pressure and laminar flow of the blood. The advantages of the helix reservoir filled with blood as opposed to a simple vertical settling column of equal height and volume for the rapid, effective, and dependable removal of any free gas which may remain in the blood after the oxygenation process are as follows: The effects of hydrostatic pressure would be the same in both systems if they were of equal heights, and if the volume of each were the same, each would have the same time interval for the separation of free gas. But, in the helix, because of the downward blood flow in the long inclined slope, the blood containing free gas, which is of a lesser density, laminates upward at the top portions of the coil while the heavier gas-free blood after a short distance flows beneath and continuously pushes this less dense (bubble containing) blood upward. In the vertical separating chamber no effective laminar flow exists, and the hydrostatic force pushing the lighter blood upward is actually opposed by the downward momentum of the heavier blood descending from above. Thus, free gas bubbles may be trapped, carried through the vertical column and embolize especially at higher rates of flow. As the evacuation rate of the reservoir becomes more rapid, then this danger inherent in the vertical settling chamber increases whereas the rapid and safe separation of the gas-containing blood remains dependable in the helix reservoir since the effective physical forces are synergistic and not opposing. As a result, the safety factor of the helix reservoir in effectively preventing air embolism is many times that of the vertical separation chamber. Thus, with the helix reservoir bubble traps are unnecessary and actually are undesirable because of their tendency to induce turbulent flow.

The apparatus is primed with a quantity of blood sufficient to give a 1 minute circuit time as this amount has provided a wide margin of safety in actual application. As general experience has indicated that the blood volume being replaced to the oxygenator from the patient is at times highly variable we have preferred not to let this venous return determine the actual amount of arterial blood delivered to that patient. We have endeavored to provide the patient with a constant known amount of arterial blood utilizing a quantity which has been proved safe.

Because of the safety factors inherent in the design of the helix reservoir, its volume may be altered significantly without danger, thereby insuring the patient a constant known arterial perfusion rate. Moreover, if venous return at any given moment decreases significantly; it is readily augmented from an exogenous source until proper venous return can be re-established.

As we have observed that hypothermia impairs the efficiency of the heart and predisposes to arrhythmias, we have preferred to maintain normal body temperatures during the perfusions. Many methods of maintaining the animal's body temperatures were tried, but the most satisfactory was that of placing the helix reservoir in a constant temperature water bath. This method has provided complete control of body temperature during the perfusions.

Short acting anesthetics in minimal amounts are desirable in studies of this nature. We have observed transient neurologic damage using a vertical reservoir or improperly designed connectors that disappeared within 24 hours after which time the animal appeared normal. The use of a long acting anesthetic would have obscured this observation. It is also true that if the animal is awake very soon after the procedure many possible postoperative complications are minimized.

The perfusion rates used in these experiments varied from 16 to 50 cubic centimeters of blood per kilogram body weight per minute. The positive action cam actuated pump used to propel the blood was calibrated in an open system using sterile saline. During the perfusion, however, the arterial pump propels against the systemic pressure of the patient. These pressures are somewhat reduced from normal, but this pump consistently delivers its calibrated volume at all perfusion rates against a pressure of 100 millimeters of mercury, which is a practical level to maintain the systemic pressures during the perfusion. In previous experiments (15) the pump did not show any variation in its output pumping either blood or saline.

TABLE III.—RESPONSES OF 22 DOGS DURING THE FIRST 2 HOURS AFTER THE PERFUSION

	Mean arterial pH	*Mean lactic acid, mgm. per cent*	*Mean w.b.c.*	*Mean platelets 1,000*
Controls* .	7.60	23	8,800	290
Final.....	7.33	44	5,200	112
½ hour...	7.36	—	7,500	176
1 hour....	7.33	36	11,000	209
1½ hours.	7.34	—	14,000	238
2 hours...	7.38	33	—	—

*Preperfusion after hyperventilation with the chest open. Perfusion rates between 16 and 25 c.c./kgm./min.

Acid base shifts were observed in these animals as a result of their perfusions, but in no instance did it seem responsible for failure of the experiment. These shifts were well tolerated by the animals and in the postoperative interval they quickly and spontaneously returned to normal levels. In the original analysis of the data it was apparent that the degree of plasma bicarbonate depression observed in these animals was greater in the group that received the lowest perfusion rate. The two groups receiving the lowest perfusion rates, however, involved the smallest animals. These data also showed that the animals within each of the perfusion groups developed approximately the same total degree of plasma bicarbonate depression regardless of size, that is to say, the smallest animals in each perfusion group showed the same degree of acid-base shift as did the largest. It was therefore apparent that the smaller dogs developed a greater plasma bicarbonate depression per kilogram body weight or per square meter surface area when compared to the larger animals. Plotting these data in Figure 3 shows that the described metabolic shift occurred directly in relationship to the animal's size as well as to his perfusion rate. The best explanation for this observation is that the smaller animals in this study were younger animals in as much as a similar relationship has been observed in the human studies (3, 4). However, no "pups" were used in any of these experiments.

The animals receiving the 2 lowest perfusion rates studied, developed the lowest arterial *p*H values. Above the perfusion rate of 25 cubic centimeters of blood per kilo-

gram per minute the observed mean arterial *p*H values were between 7.34 and 7.38. The venous oxygen saturation increased in direct relationship to the perfusion rates in these experiments, however, no such close relationship existed with the other biochemical changes studied. For human perfusions we recommend flow rates (3, 4) well above this experimentally established safe minimum value to obviate any difficulties ascribable: to biologic variations, to the varying clinical conditions present in the patients with cardiac disabilities, or to the fact that human perfusions are not of predictable duration.

Penrod found the mean oxygen consumption rate at 35 degrees in dogs to be 5.6 cubic centimeters of oxygen per kilogram body weight per minute. Most of the animals in these experiments failed to use this amount of oxygen during the perfusion interval, however, it is known that barbiturate anesthesia, which these animals received, will reduce the oxygen consumption rate by as much as 25 per cent. Helmsworth observed in dogs mean oxygen consumption values during perfusion at temperatures between 27.8 and 32.5 degrees C. and using perfusion rates between 79 and 144 cubic centimeters per kilogram per minute to be 3.67 cubic centimeters of oxygen per kilogram per minute.

It would seem that these animals may have developed some oxygen debt over the perfusion interval; however, no control observations were made of their normal oxygen consumption rate prior to the perfusion. The oxygen debt that these animals may have developed was well tolerated, an observation that was further evidenced by their normal appearance and actions after the procedure. Moreover, it is well known that a considerable oxygen debt can occur, such as in vigorous exercise, and be well tolerated. This oxygen debt will produce an elevated blood lactic acid which these animals showed (Table III); however, the adrenalin effect alone is also known to elevate the blood lactic acid and certainly considerable stress stimulating adrenalin production must be present during total body perfusion.

Four experiments, not noted in Table III, were conducted at perfusion rates above 30 cubic centimeters of blood per kilogram per minute in which serial *p*H determinations were made in the postoperative interval. In these experiments the arterial *p*H values were normal within 2 hours after the perfusion and remained in the normal range when periodically tested over the 24 hour period after the by-pass. As judged by *p*H determinations normal blood and tissue homeostasis had returned within 2 hours after by-pass.

As Figure 4 demonstrates, an increase in the perfusion rate was followed by an increase in the oxygen consumption rate up to 25 cubic centimeters of blood per kilogram per minute, but above this blood flow rate no additional oxygen was used by the animal in spite of the larger amounts of oxygenated blood supplied. The oxygen consumption rates of these animals were plotted in relationship to their surface area and their perfusion rate; however, the size of the animal seemed to have no demonstrable relationship to the amount of oxygen used during the perfusion, a finding which was contrary to that seen in humans (3).

Perfusions in the range of 40 cubic centimeters per kilogram per minute maintained a systemic pressure of about 90 millimeters of mercury which would seem to be an ample minimum perfusion pressure for the body and its organs. A decrease in the heart rate was routinely observed and is illustrated in Figure 5. A respiratory acidosis will produce bradycardia; consequently it may be supposed that a depression of the plasma bicarbonate or a metabolic acidosis also has this effect. During the heart-lung by-pass the venous inflow to the heart is obstructed. As a decrease in the venous filling of the heart produces a bradycardia this may represent another cause of the slowed heart rate observed during the perfusion.

The consideration whether or not to humidify the oxygen used in the oxygenator is readily answered by reference to the handbook of chemistry and physics by Hodgman. The concentration of water vapor

in saturated air at 38 degrees C. is 45.75 grams of water per cubic meter of air. During a perfusion of 1 hour using 10 liters of oxygen per minute, 600 liters of oxygen would pass through the blood and become saturated. Only 27 grams of water would be removed from the blood during this interval. This amount of dehydration was not believed to be consequential.

Hemolysis as a result of these perfusions was generally well within the range of safety; however, several factors became apparent during the development of the perfusion technique which decreased hemolysis when incorporated into later designs.

A leucocytosis is a response to perfusion which is in accord with the finding of Spreng.

We were unable to demonstrate damage to the erythrocytes except as measured by plasma hemoglobin concentrations. The red cell fragility tests did not demonstrate increase fragilities as a result of the perfusion, but the mechanics of the perfusion could have more subtle effects on the red cells such as diminishing their life span.

As a leucocytosis is present it may be assumed that a general response of the blood-forming elements occurs. This may be the mechanism which produces such a rapid rise in the platelets following the perfusion. Scalabrino and associates report that heparinization in a healthy person will reduce platelet counts by as much as 40 per cent. During the by-pass there is a significant heparinization present which is reversed at the termination of the perfusion. Parallel to this reversal the platelet counts rise. Two possibilities exist. The platelets may be removed from the blood by the perfusion apparatus followed by stimulation of the marrow to rapidly replace the lost platelets, or heparinization of the blood sequestrates the platelets within the body which are released back to the circulation when the heparin effect is removed. No doubt, both occur.

SUMMARY

A perfusion apparatus for open intracardiac surgery at normal body temperatures was developed which has now found extensive clinical application. The animal experimentation is described which led to the development and refinement of the apparatus. These animals were perfused with blood volumes considerably less than their cardiac output, the volumes varying from 16 to 50 cubic centimeters of blood per kilogram body weight per minute. Studies are currently in progress to evaluate perfusion rates between 50 and 100 cubic centimeters per kilogram body weight per minute. These data are being supplemented by studies in human adults undergoing reparative open heart surgery. The selected perfusion rate was maintained constant throughout the entire experiment. A decrease in the plasma bicarbonate of these animals was generally associated with the perfusion. This decrease appeared to be related to the size of the animal as well as to the particular perfusion rate. Increasing the perfusion rate served to increase the venous oxygen saturation but did not alter significantly the plasma bicarbonate depression or the oxygen consumption rate in the animals receiving more than 25 cubic centimeters of blood per kilogram body weight per minute. These observations are based upon by-pass intervals of 20 minutes, and do not apply to perfusion intervals of 20 minutes to 2 hours now under study.

All the conduits, especially beyond the filter of the oxygenator, must have uninterrupted laminar flow as any interruption in this flow, as by irregularly shaped connectors, will produce leucomoid clots of fibrin if the perfusion rate is sufficiently rapid. This factor is the usual cause of the "defibrination syndrome" (abnormal hemorrhage, neurologic damage). In all the successful experiments the animals tolerated the procedure without harm. In the unsuccessful experiments, resulting in injured animals, the causes of failure were determined and eliminated in subsequent experiments.

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DIRECT VISION REPAIR OF INTRACARDIAC DEFECTS UTILIZING A ROTATING DISC RESERVOIR-OXYGENATOR

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DIRECT VISION intracardiac surgery utilizing a pump-oxygenator for the repair of congenital cardiac anomalies has become an accepted surgical technique and is being utilized by an increasing number of cardiac surgeons. Many pump-oxygenator systems have been devised. Probably the most widely used are various modifications of the bubble oxygenator of DeWall, popularized by Lillehei and Varco (3). Kirklin has utilized the Gibbon type pump-oxygenator satisfactorily in a large number of clinical cases, and in the present series a rotating disc reservoir-oxygenator was used. It has become apparent that the acquisition of a satisfactory heart-lung machine fills only one basic requirement for successful direct vision intracardiac surgery. The others involve extensive experience in perfusion methods, perfection of intracardiac surgical techniques, and appreciation of associated clinical problems in the immediate postoperative period.

The present report is based on an experience with 45 patients operated on between January 1, 1956 and November 1, 1956 (Table I). The patients were between the ages of 1½ and 40 years weighing from 14½ to 116 pounds. The indications for surgery in each case have been based on such clinical findings as limitation in growth and physical activity, changes in cardiac status shown by electrocardiogram and roentgenogram, or on markedly elevated intracardiac pressure.

THE PUMP-OXYGENATOR

The pump oxygenator has been described in detail elsewhere (1). Its essential components are a Sigmamotor pump and a rotating disc type reservoir-oxygenator. The basic mechanism of the oxygenator is a series of 59 silicone-coated stainless steel discs supported horizontally in a pyrex cylinder coated with silicone resin. Blood introduced at one end of the cylinder is removed from the bottom of the opposite end. The rotation of the discs effectively prevents the channeling of blood along the bottom of the cylinder. With oxygenator primed with 1,400 cubic centimeters of whole blood and the discs rotating at a rate of 120 revolutions per minute, there is an exposure area of 108 square meters per minute. A mixture of oxygen and 1½ per cent carbon dioxide, warmed in a sand bath heated by an electric mantle, is supplied through a perforated stainless steel tube mounted within the cylinder above the discs. The oxygenator itself is warmed by a wrapping of silicone rubber-coated resistance wire, the temperature of which is controlled by a variac. Provision is made at the inlet face of the oxygenator for filling prior to use, the addition of blood to the cylinder during a run, and the sampling of venous return to the oxygenator from the patient. The output face is provided with openings to vent off the circulating oxygen mixture, for the collection of samples of oxygenated blood, and to receive a thermocouple for the continuous monitoring of blood temperatures. A defoaming chamber is attached to the input end of the oxygenator cylinder into which collected coronary sinus blood is pumped by means of a second Sigmamotor pump.

PERFUSION TECHNIQUES

All operations have been done with two surgeons carrying out specific tasks simul-

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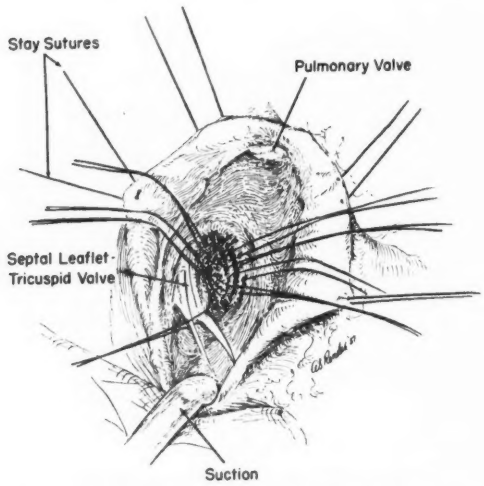

FIG. 1. Ivalon sponge disc partially sutured into a large ventricular septal defect. The septal leaflet of the tricuspid valve is retracted for proper exposure.

taneously up to the intracardiac part of the procedure, when one or the other takes over the repair of the intracardiac defect. After the heart is closed, they again work simultaneously to the end of the procedure. In this way the uncomplicated case is easily done in 2½ hours. The routine transsternal incision through the fourth interspace bilaterally is made in most instances. All cannulations are made with specially constructed cannulas of polyethylene. Arterial pressures are continuously monitored by means of a cannula in a superficial femoral artery and central venous pressures by one in the superior vena cava. Both are connected to mercury manometers. The saphenous vein is cannulated for blood replacement purposes. Arterial inflow cannulas are placed in either the left subclavian artery or superficial femoral artery. By inserting the arterial catheter in a superficial femoral artery or the right subclavian artery in the patients with a preoperative diagnosis of uncomplicated atrial septal defect, it is possible to repair the defect through a right thoracic approach, thereby avoiding a bilateral thoracotomy incision. Since there is frequently a blood pressure fall due to partial obstruction of the superior and inferior venae cavae associated with the placement of the catheters in these vessels, they are the last to be inserted after all else is in readiness for the by-pass. Prior to insertion of the caval catheters, the right atrium is explored by finger palpation to rule out the presence of an unsuspected atrial septal defect.

Early in the series perfusion rates of 40 cubic centimeters per kilogram per minute were employed but recently the rates have been generally 50 to 80 cubic centimeters per kilogram per minute. Twenty milligrams of vasoxyl may be added to the oxygenator blood to prevent the intial blood pressure drop that frequently accompanies the start of the perfusion. Attempts at maintaining high arterial pressures by increasing perfusion rates have not been uniformly successful.

Continuous monitoring of central venous pressure and maintaining it at the preperfusion level have constituted the greatest aid in achieving a balanced perfusion during the periods of cardiac by-pass. As central venous pressure rises, the rate of venous return to the oxygenator is speeded up; and as central venous pressure falls, the venous return is slowed. The amount of blood in the cavae for return to the oxygenator is inversely proportional to the extrinsic blood loss and to the amount of blood returned to the oxygenator by way of the coronary sinus suction line. Extrinsic blood loss is continuously recorded and an attempt is made to replace it volume for volume by means of the cannula in the saphenous vein. Any unmeasured extrinsic blood loss or reflex vasodilatation resulting in decreased venous return to the cavae and a concomitant decrease in the venous return to the oxygenator automatically is compensated for with blood from the reservoir-oxygenator, and is measured as a fall in the oxygenator blood level. In this way the central venous pressure acts as a fairly accurate index of the circulating blood volume in the patient. After cardiotomy closure the caval tapes are released and the pump rate de-

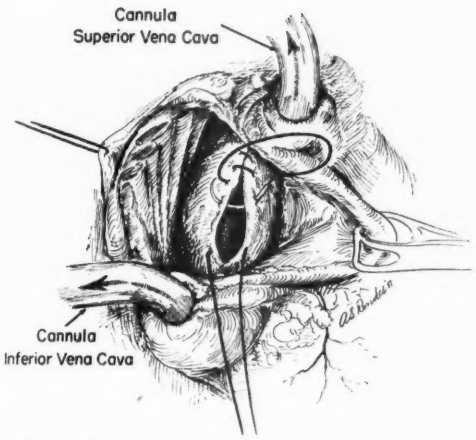

FIG. 2. Illustration of the excellent exposure obtained during closure of an atrial septal defect by means of direct vision surgery with a pump oxygenator. The level of blood in the left atrium is maintained at the mouth of the defect to prevent air embolization to the left side.

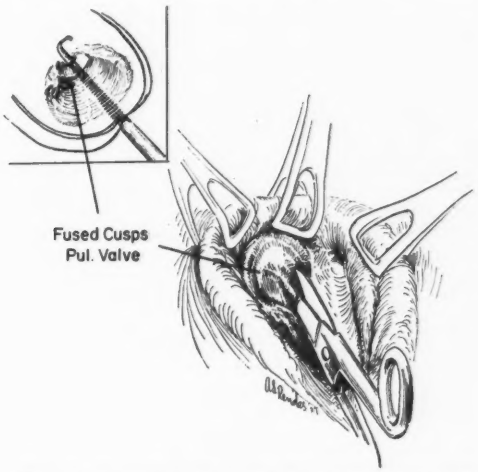

FIG. 3. Correction of a valvular pulmonic stenosis through the right ventricular approach by retracting the pulmonic valve into the right ventricle. The valve is then cut along the lines of the fused commissures and the fibrous tip cut off, if necessary.

creased slowly, maintaining a satisfactory central venous pressure and systemic arterial pressure until the heart takes over satisfactorily. The patient is weighed immediately postoperatively, and the weight is adjusted by means of blood transfusions, or blood removal if necessary, to correspond to the preoperative weight taken just prior to surgery. If the precautions as outlined are taken during the period of perfusion, preoperative and postoperative weights correspond very closely.

INTRACARDIAC TECHNIQUES

A dry operative field is mandatory for proper identification and repair of intracardiac defects. This has been obtained by means of a sump-type suction tip in the heart, connected to a Sigmamotor pump to return the coronary sinus blood to the oxygenator. Because of the uniformly poor experience resulting from the use of potassium citrate induced cardiac arrest and coronary artery inflow stasis in the laboratory, this technique has not been employed extensively clinically in order to obtain a dry operative field.

The greatest experience to date has been in the repair of ventricular septal defects, auricular septal defects, and pulmonic stenosis, alone or in various combinations. Ivalon sponge prostheses have been used in the repair of the larger ventricular septal defects; whereas, the smaller defects have been closed by interrupted sutures of No. 000 silk (Fig. 1). Several techniques have been described for suturing the ivalon sponge into the defect. We merely have anchored it with a few mattress sutures supplemented by small interrupted sutures about the periphery. This method has worked satisfactorily, and the blood clotting in the interstices of the ivalon sponge seems to aid in sealing off any small residual openings between the stitches.

Atrial septal defects have been closed by direct suture by use of either interrupted sutures of No. 000 silk, or a continuous suture reinforced with interrupted sutures (Fig. 2). Special techniques, such as ventricular fibrillation or the placement of a vent in the left ventricle, which have been described for the prevention of air emboli, have not been utilized. The patient is positioned

TABLE I.—FIRST 45 CASES

*Defect**	*No.*	*Survival*
Ventricular septal defect	16	13
With atrial septal defect	1	0
With anomalous pulmonary drainage into coronary sinus	1	0
With patent ductus and congenital mitral insufficiency	1	0
Tetralogy of Fallot*	6	5
Pentalogy of Fallot	1	0
Atrial septal defect	8	7
Valvular pulmonic stenosis	6	6
Transposition of great vessels	2	0
Atrioventricular communis	1	0
Exploratory cardiotomy	2	2
	45	33 (73%)

*All patients with ventricular septal defect and pulmonic stenosis were placed in this group. Four had significant arterial desaturation, and 2 did not.

so that the left atrium is as dependent as possible and the level of blood in the left atrium is maintained just at the rim of the atrial septal defect through judicious use of the sump suction. Air is thus prevented from gaining entrance to the left side of the heart and the technique is not a complicated procedure.

Pulmonic stenosis has been approached from the right ventricular side rather than through the pulmonary artery (Fig 3). It is believed that this approach is advantageous in that other defects, such as an associated infundibular stenosis or a ventricular septal defect, can be identified easily, and repaired if present. To correct a valvular pulmonic stenosis, the ventriculotomy incision is placed higher on the pulmonary outflow tract than usual, just proximal to the pulmonary valve annulus. A nerve hook is passed upward through the stenotic valve orifice, and the cone-shaped valve is easily inverted and retracted into the ventricle. It is then a simple task to open the stenotic valve by cutting along fused commissures with a scissors and convert it under direct vision to a bicuspid valve. The fibrous tip of the funnel-shaped valve may be cut off if deemed necessary. Two cases with valvular pulmonic stenosis have had an undiagnosed associated lesion which may have been missed, or would have required a second incision into the ventricle if the valve had been approached through the pulmonary artery.

PHYSIOLOGIC DATA

Complete physiologic data have been analyzed concerning the first 40 patients operated on to date. Blood flow rates utilized were 40 to 115 cubic centimeters per kilogram per minute, and with these flow rates average mean arterial blood pressures ranged from 38 to 86 millimeters of mercury (average 61 mm. Hg). One patient was carried with an average mean arterial blood pressure as low as 38 millimeters of mercury for 106 minutes with no apparent ill effects. The clotting mechanism has not been disturbed, the clotting time being returned to less than 15 minutes in all but 3 of the cases immediately postoperatively by giving protamine sulfate in a dose calculated to be one-half of the initial heparin dosage. Platelet counts remained above 120,000 except in 4 instances. In 10 cases in which they were measured, there was no significant change in the plasma fibrinogen or the clot lysis. Blood destruction has been minimal. There has been little change in the formed elements of the blood, and the average increase in plasma hemoglobin during perfusion periods, ranging from 12 to 106 minutes, has been 53.5 milligrams per cent. The highest figure obtained was a plasma hemoglobin of 320 milligrams per cent, much of which came from the sump suction. The patient recovered from the procedure with no ill effects resulting.

The hydrogen ion concentration of the arterial blood during the by-pass periods ranged from 7.14 to 7.62, the majority being between 7.3 and 7.4. There has been no significant change in the carbon dioxide content, during or after a run, when 1½ per cent carbon dioxide is added to the oxygenator. A slight metabolic acidosis exists during the perfusion period which corrects itself rapidly post-perfusion. All blood studies have continued to be normal during the entire postoperative periods. Arterial oxygen saturation has ranged from 95 to 103 per cent except in 2 cases in which it was 92 and 93 per cent. The venous oxygen saturation ranged from 33 to 58 per cent. Blood bal-

TABLE II.—ANALYSIS OF DEATHS

Case No.	*Defect*	*Right ventricle systolic pressure*	*Arterial oxygen saturation, per cent*	*Comments*
4	Ventricular septal defect with pulmonic stenosis	88		Poor surgical risk Difficult anatomic defect
6	Ventricular septal defect	88	91.0	Very poor surgical risk Preoperative atelectasis and pulmonary edema
10	Ventricular septal defect with pulmonary venous drainage into coronary sinus	76	91.4	Incomplete correction of anomaly
18	Atrial septal defect	40	43.6	Good surgical risk Defect easy to close
19	Transposition of great vessels	92	24.1	Difficult anatomic defect
22	Transposition of great vessels			Difficult anatomic defect
23	Ventricular septal defect with patent ductus and congenital mitral insufficiency	76	81.3	Difficult anatomic defect Heart block postoperative
24	Ventricular septal defect	90	95.0	Difficult anatomic defect Postoperative bleeding
27	Atrioventricular communis	96	87.6	Poor surgical risk Difficult anatomic defect
28	Atrial septal defect Ventricular septal defect	60	95.3	Previous cardiac surgery Difficult dissection
31	Atrial septal defect Ventricular septal defect, hypoplastic pulmonary artery Infundibular stenosis	84	68.0	Difficult anatomic defect Hypoplastic pulmonary artery comprised procedure
38	Ventricular septal defect	110	93.0	Markedly increased pulmonary vascular resistance

ance during the operative procedure was well maintained in that all but 3 of the 40 postoperative weights were within ¼ pound of the preoperative weight. This has been corroborated by normal postoperative hemoglobin and hematocrit values. All in all, the oxygenator has functioned satisfactorily from a physiologic standpoint in the clinical cases done to date.

RESULTS

The mortality in the 45 cases was 27 per cent, 33 of the 45 patients surviving surgery (Table I). This mortality may be corrected to 23.2 per cent, however, if the 2 cases of transposition of the great vessels are excluded from the series, since operation was performed in spite of a known high operative risk in order to test a new surgical principle in their repair. The operative mortality in patients with only a ventricular septal defect was 19 per cent, 13 of 16 patients surviving. There was 1 death in 8 patients undergoing repair of an uncomplicated atrial septal defect and no deaths in the 6 patients with uncomplicated valvular pulmonic stenosis. The records of the 12 patients who died have been studied carefully in order to pinpoint a specific cause of death. Two died postoperatively while still in the operating room after multiple episodes of cardiac arrest. In 1 case the heart was restarted 9 times before final failure. The other patient had a conduction defect resulting from surgery, which undoubtedly contributed to the inability of the heart to take over postoperatively. Eight of the other 9 patients died within the first 24 postoperative hours, most of them starting to have trouble in the first 12 hours. It is difficult to assign a specific cause of death in each instance. With 1 exception all of the deaths occurred in poor risk patients, or in those in whom the anatomy of the defect presented difficult problems related to proper correction (Table II). No deaths can be ascribed to the pump-oxygenator per se. Pulmonary complications were by far the most frequent postoperative problem. Two patients required emergency tracheotomies in order to aspirate the excessive pulmonary secretions; in 1 patient with a preoperative atelectasis, and with pulmonary edema noted at surgery, the tracheotomy was done prophylactically. Furthermore, the only positive finding at postmortem in 3 of the children

who died was pulmonary edema, with or without associated atelectasis. One child developed a left chylothorax, and another thrombophlebitis. There was one episode of successfully treated cardiac arrest occurring in the recovery room in a child with an uncorrectable defect. The same child later developed a cerebral thrombosis with a residual paralysis. It is believed there were no more postoperative complications in these cases in which the pump-oxygenator was used than might occur in patients of similar risk if closed cardiac techniques were employed. It is believed, however, that the transsternal incision probably is not as well tolerated as the usual unilateral thoracotomy incision, and that pulmonary complications, therefore, have to be guarded against more stringently.

All but 1 child surviving surgery are living, and are well with the exception of the child who developed the cerebral embolus 1 month postoperatively. Surgery has been done too recently in the majority of these cases to discuss results in terms of clinical improvement, or physiologic improvement as evaluated by recatheterization studies.

SUMMARY AND DISCUSSION

There can be little doubt that the future of cardiac surgery lies in the further development of safe direct vision techniques. The advantages of the open techniques are obvious: (1) easy visualization of all valves, septa, and chambers; (2) complete correction of existing defects when possible; (3) identification and repair of associated defects previously undiagnosed. For instance, in 2 patients operated on for valvular pulmonic stenosis, associated ventricular septal defects were found and corrected, and in 1 there was also an unsuspected infundibular stenosis.

Where there has been an opportunity to compare open techniques with previously tried closed techniques, the former have proved eminently more satisfactory from all standpoints. Two atrial septal defects incompletely closed by a closed technique have now been completely closed by open surgery. With 1 exception, good to fair risk patients with anatomic defects easy to correct have done well, and it has been the poor risk patient, or the one with a complicated defect, that has not survived surgery. This observation perhaps indicates that the time is approaching when atrial septal defects and ventricular septal defects will be viewed as a patent ductus arteriosus is viewed at the present time; that is, when the optimal time for surgery is reached it is carried out electively rather than waiting for the individual to develop significant symptoms. This accomplishment should be the ultimate goal of all cardiac surgeons.

Emphasis is placed on the use of extensive physiologic studies before, during, and after the period of cardiac by-pass, for it has been through the analysis of these studies that we have been able to continue to refine our techniques in direct vision surgery. It should be stressed again that a satisfactory pump-oxygenator is only part of the formula for success. With such machines becoming available in increasing numbers, the rest consists of extensive teamwork in the preoperative techniques, and intensive care and observation postoperatively, especially in the first 24 hours.

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CYTOLOGIC AND HISTOLOGIC CORRELATION OF COLPOSCOPIC FINDINGS

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BIOPSY is the final definitive method for the evaluation of cervical lesions. A well recognized, accessory measure of proved value is the cytology smear. At our institution we have been interested in colposcopy, a means of cervical portio scanning described over 30 years ago by Hinselmann of Germany.

Colposcopy may be defined as magnified stereoscopic visualization of an organ surface with direct illumination. The colposcope is usually directed to the portio of the uterine cervix but it has been utilized to assess vaginal and vulvar changes as well. The findings noted by colposcopy depend on two sets of factors: (a) epithelial: cell type (i.e., squamous or columnar), thickness of epithelium, keratosis and parakeratosis, total nuclear substance, and growth pattern; and (b) vascular: intensity of vascularization and character of the individual superficial vessels.

The relationships of the three investigative methods of colposcopy, cytology, and biopsy need further exploration. Some papers, mainly in the foreign literature, have appeared on various aspects of this subject; our own data on the relationships between cytology and colposcopy have previously been reported (2, 3).

MATERIAL AND METHODS

We have practiced colposcopy at our institution for more than 3 years. During that time, approximately 1,000 colposcopic examinations have been performed. Although the number is small in comparison with the figures of some European clinics the examinations have been carried out by a small team of individuals and have been carefully documented with regard to history, gross appearance, and the cytology and biopsy findings.

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We have utilized exclusively a binocular colposcope mounted on an adjustable stand with a built-in Leica attachment that uses the lens system of the colposcope for the taking of kodachromes. Magnification is adjustable to 10× or 20×; we prefer the former. A monochromatic green filter is easily adjusted into place; this is especially valuable in studying the three types of leucoplakia, and blood vessel patterns. The technique of colposcopy is outlined as follows:

1. Insertion of speculum
2. Adjustment of colposcope
3. Inspection of cervical portio
   a. In situ
   b. After gentle cleansing
   c. After 3 per cent aqueous acetic acid
   d. After aqueous iodine (Lugol's) solution
   e. Green filter as required
   f. 10× or 20× magnification

The majority of the cytologic smears in this study are cervical scraping smears taken either with a wooden spatula or a cotton-tipped applicator; some smears are vaginal. The smears have been fixed in equal parts of 95 per cent alcohol and ether, then stained by the method of Papanicolaou.

Biopsy has been carried out in practically every instance of an abnormal smear or of an abnormal colposcopic picture. The biopsies were either cone biopsies, often with a given abnormal area excised separately; or spot biopsies taken of unusual epithelial areas. Fractional curettage was also done on hospitalized patients.

COLPOSCOPIC CYTOLOGIC HISTOLOGIC RELATIONS

Benign findings. There are three major benign findings on the ectocervix noted by the colposcope. First, the portio may be intact, covered solely by squamous epithelium. Such epithelium stains brown on the application of aqueous iodine (Schiller test); occasionally there is a fine stippling consisting of tiny noniodine staining areas. Normal squamous cells are found in the smear, and biopsy demonstrates multilayered squamous epithelium overlying connective tissue.

The second benign finding has been designated as *ectopy* by Hinselmann and consists of a perioral rim of columnar epithelium around the anatomic external cervical os. It corresponds to the so-called "congenital pseudoerosion" occurring mainly in girls and young women. This area of ectopy appears reddened by gross inspection and does not take the iodine stain. Colposcopically the columnar epithelium is pale, bubbly, and grapelike. These characteristics are accentuated by the addition of 3 per cent acetic acid. Typical columnar cells are found by cytology smears; columnar epithelium, with glands reaching into the stroma, is noted by biopsy.

By far the most frequent benign abnormality of the portio is the transformation (regeneration) zone. This consists of a mixture of both columnar and squamous epithelium. Here one sees islands of columnar epithelium, gland openings in fields of squamous epithelium, and dilated glands (nabothian cysts). Grossly, the cervix is said to be "eroded." The iodine stain is often poorly taken by the regenerating squamous epithelium. Normal columnar and squamous cells are usually desquamated but since this zone represents a healing process, atypical cells may be shed as well. Histologically, normal columnar and squamous epithelium, and often epidermidalization, are seen. The cytologic and histologic patterns of the three major benign findings are diagrammed (not according to scale) in Figure 1.

There are some reactive portio changes of benign nature that warrant consideration. With procidentia the epithelium becomes thickened taking the iodine stain poorly; the smear shows increased cornification, and keratosis or parakeratosis is found by biopsy. With *estrogen deficiency* the epithelium becomes thinner than usual. Colposcopically, tiny petechial hemorrhages, and occasionally small ulcerations are noted; iodine staining is poor; the characteristic atrophic smear and the thin-layered epithelium noted on biopsy are well known. The colposcopic portio changes of Trichomonas vaginalis infestation consist of clusters of petechial hemorrhages. We have also noted a patchy ring type of leucoplakic change, the "rings" being about 1 or 2 millimeters in diameter. The cytologic smears may demonstrate increased nuclear activity and cytoplasmic vacuolization; biopsy shows an epithelial and stromal inflammatory process. During pregnancy, columnar epithelium, viewed by the colposcope, seems to proliferate, becoming hyperplastic and polypoid; the squamous epithelium hypertrophies. The portio almost invariably demonstrates a vascular, succulent transformation zone. Cytologic scrapings in such instances are usually normal. Biopsy, of course, shows the changes of pregnancy.

Abnormal findings. Because of increased opacity, abnormal epithelium may appear whitened when viewed by the colposcope. Such an area, in colposcopic terminology, is then said to be an area of leucoplakia. Three varieties of colposcopic leucoplakia are described: simple leucoplakia; mosaic leucoplakia; and ground leucoplakia. Each of these three remains unstained after the application of aqueous iodine solution; 3 per cent aqueous acetic acid increases delineation.

Simple leucoplakia may be easily visible by naked eye inspection. On the other hand, it may be so tiny that it is detected only by magnification. In either case it resembles leucoplakia as we know it elsewhere in the body. Cytologically, since the surface is so

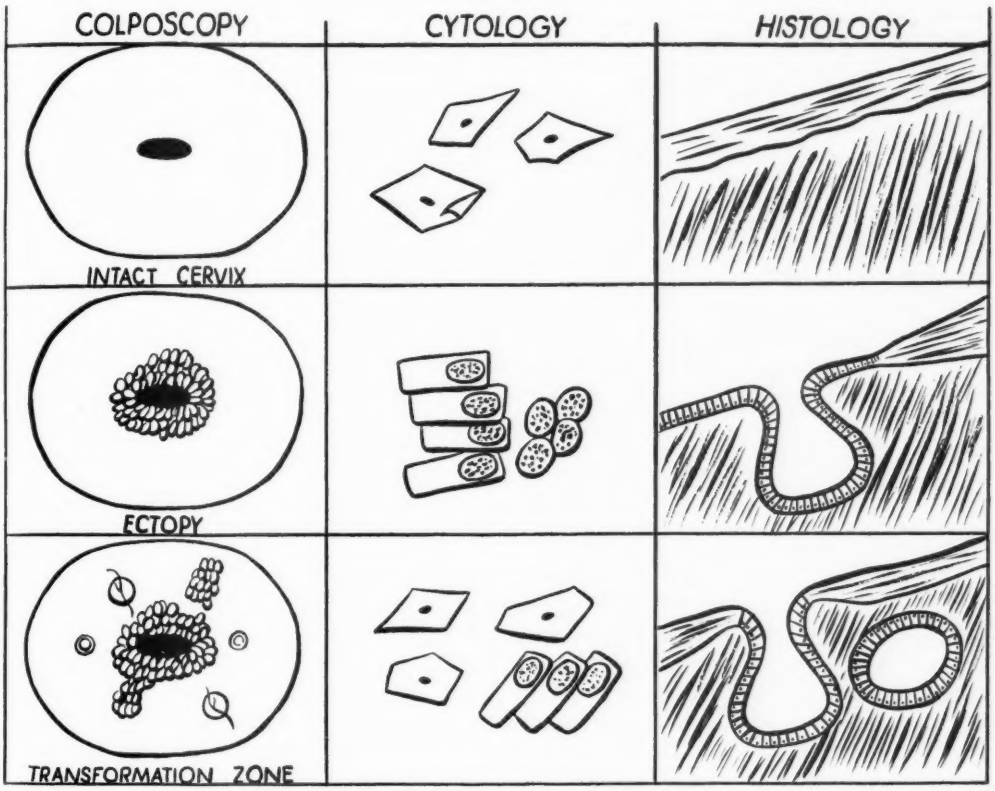

FIG. 1. Diagram (not according to scale) of cytologic and histologic patterns showing correlation of three major benign colposcopic findings (see text).

often keratotic or parakeratotic, there is an increase of cornified cells in the smear.

Leucoplakic spots may assume a mosaic pattern (mosaic leucoplakia) or a stippled pattern (ground leucoplakia). Such regions of colposcopic atypism are pinker than simple leucoplakia. The growth of epithelial pegs and connective tissue septa account for these colposcopic pictures. Mosaic and ground leucoplakia may merge, one with the other.

By the smear technique most areas of leucoplakia yield normal appearing cells. A layer of keratosis, however, may overlay atypical cells, and a false negative smear results. A number of histologic alterations may produce the optical phenomenon of decreased transparency and it should be emphasized that the leucoplakia in itself is not significant but its histologic cause is. The kinds of histologic alterations producing colposcopic leucoplakia (benign, atypical, or malignant epithelium) consist of, singly or in combination, one or more of the following: keratosis, parakeratosis, epithelial thickening (with or without peg formation), and increase of total nuclear substance. These modifications may occur with normal or abnormal epithelium. An example of leucoplakia with cancer is found in Figure 2.

On occasion one finds "silent" noniodine staining regions of squamous epithelium which otherwise appears quite normal. These may represent early "leucoplakic" changes. Here again the smear is most frequently negative but may be abnormal depending upon the histopathologic findings.

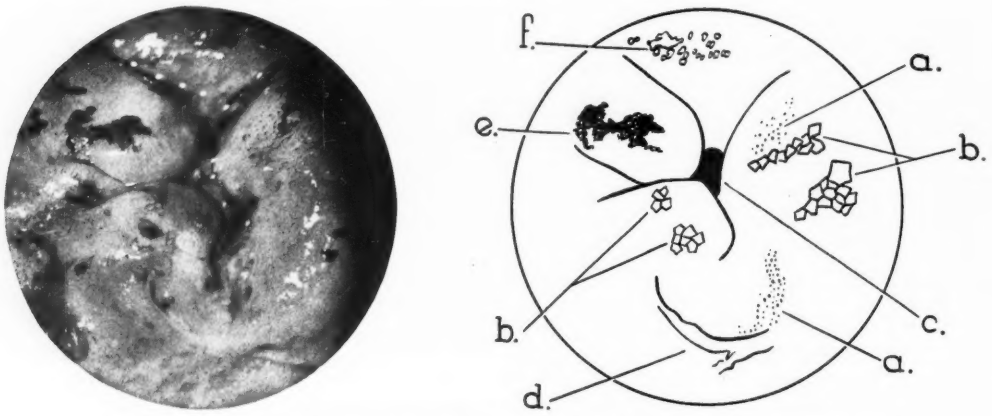

FIG. 2. Colpophotograph of leucoplakia associated with early malignancy. S. B., negress, age 30 years, gravida 1, para 1. Only symptom was slight staining. By gross inspection, cervix seemed whitened. Colposcopic findings are shown in picture and diagram (*a.*, ground leucoplakia, *b.*, mosaic leucoplakia, *c.*, external cervical os, *d.*, simple leucoplakia with irregular surface, *e.*, area of friability, *f.*, highlights). Smear classified as Papanicolaou class III. Biopsy disclosed early invasive squamous cell malignancy. Stage I lesion.

As in gross malignancy, ulceration may occur. This is known colposcopically as *true erosion.* Since loss of epithelium may be the result of trauma, atrophy, and inflammation, in itself it is not specific for malignancy. The older term for true erosion was *uncharacteristic red area* but the terms are not completely synonymous since localized vascularization with an intact epithelial surface is also found in atypism and early malignancy. Proliferation may be noted colposcopically. The accompanying vascular pattern may present a "cork-screw" or "comma" appearance with irregular vessel caliber, i.e., adaptive vascular hypertrophy. A more recently described colposcopic change is the atypical transformation zone. Such a transformation zone appears yellow and glassy; the rims of its few gland openings are coarse; abnormal blood vessels are seen. The problem cytologically as well as histologically again rests on the histologic reason for these findings. This last group of findings are probably more indicative of atypism or malignancy than the three forms of leucoplakia. In these particular instances, the smear, together with the biopsy are found to correspond appropriately.

DISCUSSION

It should be recalled that colposcopy and cytology are two different disciplines. The former evaluates epithelial architecture; the latter the unit of epithelium, the cell. Both depend upon histology. It does not seem that colposcopy and cytology need vary concurrently. Abnormal architecture may mean abnormal cells but not necessarily; on the other hand, abnormal cells are more frequently associated with abnormal histopathologic structure. To date, we have not seen any cases of abnormal portio smear without some abnormal colposcopic manifestations. Either method may miss an atypism or carcinoma which the other detects, and in evaluating a false positive smear colposcopy may indicate the site to be biopsied. As to the question of which is more reliable in cancer detection one must say that the smear is more specific for malignancy while colposcopy, by its very nature, more easily selects areas of minor degrees of atypism (3). Used together they are more efficient in the detection of early cancer.

The connotations of the term leucoplakia as used in colposcopy have been mentioned. Histologically, keratinization may or may

not be present. Increased cornification with carcinoma both cytologically and histologically has been reported. This would agree with the colposcopic concept of leucoplakia in some cases of early cervical malignancy but does not mean that these changes necessarily indicate the presence or the future development of malignancy. Reagan has called attention to the tendency toward epithelial thickening in what he speaks of as atypical hyperplasia; this would produce a colposcopic leucoplakia. He has also described the broadening and blunting of the rete pegs in this condition; colposcopically such a growth pattern is consistent with mosaic or ground leucoplakia. It is true that early malignancy may be characterized colposcopically by leucoplakic change alone (2). In general, however, most of the literature on abnormal epithelium including carcinoma in situ contains little reference to the over-all growth tendencies of the epithelium.

With benign colposcopic findings, histologic correlation is quite exact. This is not so with the abnormal ones. It is possible with experience on the basis of qualitative and quantitative colposcopic changes to suspect that a given area is malignant but as with the smear, biopsy is still mandatory before treatment. Some authors have attempted to correlate the percentage of epithelial atypia, in situ carcinoma, and invasive malignancy to be expected from the different abnormal colposcopic findings. In most such reports the majority of biopsies are benign. Ideally some sort of objective grading of colposcopic pictures is needed to help select which cases will demonstrate the more serious lesions histologically.

SUMMARY

The cytologic and histologic variations of the different colposcopic manifestations, including the three variants of leucoplakia, have been briefly reviewed. It is possible to predict somewhat the corresponding histologic makeup and thereby the smear findings. This is more easily done with normal than with abnormal colposcopic findings.

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LYMPH BORNE INFECTION AND ANEURYSM FORMATION

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LITTLE MENTION is made in standard texts of the development of aneurysms, other than those in the aorta due to syphilis, from weakening of the vessel wall by infection carried into its very substance along the lymphatics accompanying the vasa vasorum. Yet bacteria may travel by the same route and may cause serious weakness to develop quickly in a localized area of the vessel wall. In the 2 cases to be presented, it is believed that this mode of aneurysm formation had occurred. Such aneurysms tend to be saccular and their formation rapid so that surgical intervention may be needed as an emergency treatment. If the vessel involved is such that the preservation of its lumen is essential, as in our cases, then it is likely that the restorative operation will have to be carried out in an infected field. While the current trend is to use a graft for arterial replacement, it is obviously undesirable to introduce a large volume of dead organic material or inert prosthesis into tissues in the presence of infection. The treatment used consisted of excision of the aneurysmal sac and restoration of the vessel lumen by lateral arteriorrhaphy.

Of the two aneurysms now reported, one was due to tuberculosis, a very rare cause of aneurysm formation in limb arteries.

CASE 1. J. C., male aged 78 years, was admitted to the hospital at the end of November 1953, with a history of tuberculosis of the right leg which had necessitated midthigh amputation 18 months previously; a course of streptomycin and PAS had been given at this time. He remained well for a year; a tuberculous infection then developed in the ankle joint and the prepatellar bursa of the left leg. One gram of streptomycin and 12 gram of PAS were given daily for 70 days, and this therapy, together with immobilization of the limb, resulted in the infection becoming quiescent by November 1953. At the end of this month, however, it was noted that the left foot was cyanosed and cold and that a pulsatile aneurysm, 3 inches in diameter, had appeared at the junction of the middle and lower thirds of the superficial femoral artery. This observation was confirmed by arteriography which also confirmed that the profunda femoris artery did not fill and that the wall of the superficial femoral artery was grossly atheromatous, the collaterals were few and poorly filled (Fig. 1).

At this time the erythrocyte sedimentation rate was 32 and 53 millimeters in the first and second hour but the roentgenogram of the chest showed no active tuberculosis and examination of the sputum was negative, as were repeated 24 hour specimens of urine, examined for tubercle bacilli.

The aneurysm had appeared suddenly and enlarged rapidly, perhaps aided by strenuous efforts on the patient's part to "massage the lump away." Operation was obviously necessary.

Operation was carried out at the beginning of December 1953. The left superficial femoral artery was exposed in its lower part by the standard approach of Fiolle and Delmas. In the region of the sac there was considerable matting together of the parts and toward the upper pole of the swelling, which measured 4 inches in the longer axis by 3 inches, the vastus medialis was infiltrated with blood from the sac. A prominent feature was the presence of thickened, swollen lymphatic channels in and around the vascular axis. After control of the artery proximal and distal to the sac, this was opened to expose the communication with the parent trunk which was an ovoid opening a half by a quarter of an inch, surrounded by healthy intima. The fundus of the sac had no smooth endothelial lining and was rough with adherent clot and blood extravasated into its substance. The opening from the femoral artery was closed by overstitching with No. 5-0 arterial silk, the excess sac was cut off, and the remaining cuff was closed over the repaired intima with horizontal mattress sutures. During the operation, 10,000 units of heparin were instilled into the isolated arterial segment. Primary closure of the wound was carried out and anticoagulants were given, heparin for the first day or two then tromexane for a week. Convalescence was uneventful, the nutrition of the left leg and foot improved markedly and the distal peripheral pulses became easily palpable. After opera-

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tion the patient had a further course of 1 gram of streptomycin, 12 grams of PAS, and 200 milligrams of isonicotinic acid hydrazide daily for 30 days. At the end of this time he was discharged in good general health with the wound soundly healed and the femoral artery patent. About 6 months later he began to have anginal attacks and died from myocardial infarction just over a year after his operation. The femoral artery had remained patent throughout this period, and no further aneurysm had formed.

Histology. The portion of the sac wall measured 5.5 by 4 centimeters and was lined by fibrin, while externally tags of adherent muscle infiltrated with blood could be identified. Microscopically, the structure varied in different areas. Nowhere could remnants of an artery wall be identified for the sac was composed mainly of condensed collagen, 1 or 2 millimeters thick, lined internally by hyalinized fibrin undergoing organization. In other parts the layer of fibrin rested on more recently condensed connective tissue and atrophying muscle fibers. Evidence of still more recent expansion and leakage was observed where the muscle was infiltrated with blood, and small areas of ischemic necrosis had occurred in the adjacent tissues which were invaded by polymorphs. Involvement of the wall by tuberculosis was extensive (Fig. 2), and in the tissues nearby evidence of lymphatic spread could be seen (Fig. 3). The histology was typical of this disease; the lesion was chiefly proliferative but areas of caseation had occurred and acid-fast bacilli were easily demonstrated. No lymph nodes or lymphoid tissue could be found.

CASE 2. A 46 year old man, looking pale and ill, was referred on September 24, 1953 with the diagnosis of left common carotid aneurysm. Ten weeks previously, a few days after extraction of an infected left lower molar stump, he noted an acutely tender, painful swelling on the left side of the neck. As the pain subsided, he became conscious of the pulsating nature of the lump, and noted that it continued to enlarge, doubling its size in the 10 days prior to admission, during which time he became hoarse and was having difficulty in swallowing solids. He also had left sided headaches, felt ill, and was losing sleep. He was admitted to the hospital and started on penicillin and aureomycin, forthwith.

On examination there was an obvious aneurysm of the common carotid artery arising near the bifurcation. Pressure on the artery below the sac caused faintness in about 15 seconds. The sac, roughly ovoid, was overlapped by the sternomastoid muscle, and measured 2 inches in the long axis and 1½ inches transversely. The tissues in the vicinity felt indurated and were reddened and tender. A sharp snapping systolic bruit was audible on auscultation over the sac. Wassermann reaction and blood cultures were negative.

Two days after admission, angiography was carried out which showed that the aneurysm was saccular, arose from the upper part of the left common carotid

FIG. 1. Case 1. Femoral arteriogram showing saccular aneurysm, poor filling of the collaterals, and gross atheroma of arterial wall.

artery, and that there was a medial prolongation toward the hypopharynx which was displaced with the trachea across the midline of the neck (Fig. 4). By this time the patient's voice was reduced to a hoarse whisper, and he could swallow only fluids. In view of his poor state of health, the pressure effects, and the fear that the aneurysm might rupture into the pharynx, immediate operation seemed imperative and since fainting followed more than 15 seconds compression of the common carotid artery involved, it was evident that every effort would have to be made to retain the lumen of this vessel. Operation was carried out the following day. By an angled incision along the anterior border of the left sternomastoid muscle from the angle of the jaw to the sternoclavicular joint and thence just above and parallel to the left clavicle, the length of the carotid sheath was exposed by division of the lower end of the sternomastoid muscle. The surrounding tissues were adherent to the sac, necessitating tedious dissection before this was isolated (Fig. 5). The common facial and internal jugular veins were completely compressed and adherent to the sac while the left vagus nerve was spread out over its posterolateral surface. The vagus was dissected off, the adherent veins were divided, and the portions adherent to the sac were left attached thereto. The medial pro-

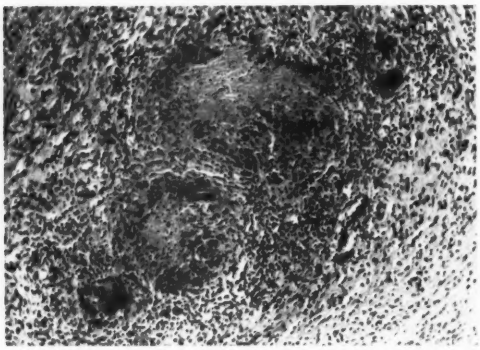

FIG. 2. Case 1. Typical tuberculous granulation tissue with foci of caseation in wall of the aneurysm sac. ×47.

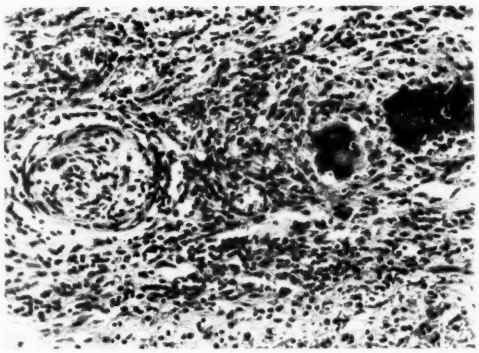

FIG. 3. Case 1. Perivascular lymphatic spread of tuberculosis in tissue adjacent to the sac. ×83.

longation of the sac toward the hypopharynx was then seen to be thin and here pus was found and a sample secured for examination; the adjacent lymph nodes were inflamed. A Potts' clamp was then applied to the neck of the sac and the latter excised. Bulldog clamps controlled the common external and internal carotid arteries after the latter two vessels had been allowed to bleed back to wash any potential emboli out, but this retrograte flow was very poor. Ten thousand units of heparin were then injected into the vessel. After the sac had been removed, it was found, on trimming the edges of the gap in the arterial wall, that this was not diseased and that the opening consisted of an almost linear slit 1 inch in length. The slit was closed with No. 5-0 silk applied as a horizontal mattress stitch, and on removing the clamps the flow through the repaired segment appeared to be excellent. The flow through the common carotid artery had been shut off for 10 minutes during the entire operation. The sutured segment was then reinforced with a wrapping of fascia lata which was stitched to itself and the adventitia of the artery. The wound was closed with a small rubber tube drain in the lower end of the wound.

FIG. 4. Case 2. Arteriogram of lateral projection of the left carotid showing saccular aneurysm arising from the upper end of common carotid artery.

Postoperatively, anticoagulants, heparin, and tromexane were given for 20 days. No signs of cerebral ischemia occurred during the postoperative period. By palpation, the common carotid artery remained patent. The hoarseness gradually disappeared, and the patient regained a good speaking voice. While the sample of pus taken showed merely polymorphs in various stages of degeneration, no organism being grown on culture, the patient was continued on penicillin and aureomycin for 10 days after operation.

Histology. The specimen measured 6 by 2.5 centimeters and showed a thin aneurysmal sac on the surface of which the portion of the internal jugular vein was adherent. Microscopic examination of transverse sections through the sac wall showed laminated thrombus on the endarterial surface and pus-infiltrated connective tissue containing necrotic collagen fibrils on the opposite surface. The inflammatory infiltration contained fairly numerous eosinophils and the tissue changes generally indicated a process of some weeks' duration. No bacteria or fungi were demonstrated by the application of special staining methods. All the small veins in the area as well as the jugular showed active intimal thickening and some inflammatory separation of the layers of the wall. Small arteries and arterioles appeared normal. Only a few elastic fibers remained in the sac wall. No lymphoid remnants were seen in the immediate area of suppuration. A node from adjacent tissue showed simple, acute, reactive changes with some fibrosis but no suppuration.

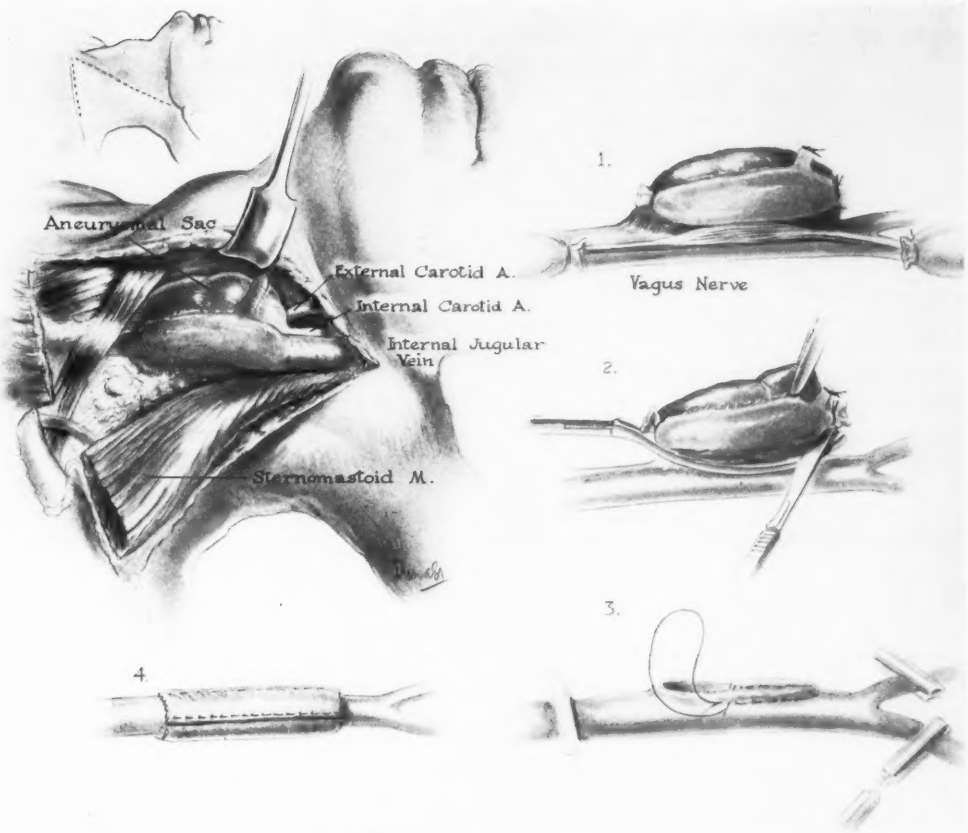

FIG. 5. Case 2. Sketch made at operation.

This patient has now been followed for over 3 years. Both carotid systems are patent with no further aneurysm formation. His general health has been excellent apart from acute cholecystectomy.

DISCUSSION

The weakening effect of a bacterial infection on an artery wall is well recognized in the etiology of aneurysms but the variety of possible pathways by which infection may reach the vessel wall is not always fully comprehended. Commonly only 2 are considered, namely, involvement of the outside of the vessel wall in an inflammation of the adjacent tissues in direct continuity with the vessel wall, and, in mycotic aneurysms, lodgment of an infected embolus in the lumen of the vessel weakening it from the inside.

Two further pathways exist which may permit the passage of infection into the substance of the vessel wall; namely, by blood borne infection via the vasa vasorum which is perhaps the true mechanism of mycotic aneurysm formation, as indicated by Cappell and by infection carried by the lymphatic channels of the vasa vasorum. Infection of the substance of an artery wall will damage the media in which the main strength of an artery lies and even limited disruption of this coat must seriously predispose to aneurysm of the saccular type.

In the 2 cases described the infection clearly arrived via the lymphatics: in Case 1 from a tuberculous synovitis affecting the ankle and prepatellar bursa of the affected

limb, and in Case 2 along the cervical lymphatics from the septic tooth socket in the lower jaw of the same side. Whether the infection settled in the substance of the vessel wall initially, or whether there was first involvement of lymphoid tissue in close apposition to the vessel with subsequent direct spread to involve the wall is impossible to state categorically; but the carotid may have been directly implicated by a suppurative lymphadenitis, for the regional nodes were inflamed and there was pus around the apex of the aneurysmal sac. In the tuberculous aneurysm it seems more likely that the infection invaded the substance of the vessel by lymphatic channels and set up tuberculomas in the wall, thereby weakening it, for there was no obviously tuberculous focus in the tissues in immediate contact with the vessel. While localized tuberculous arteritis is met with in small arteries of the brain, lung, and other viscera, the usual sequel is obliterative endarteritis. Only in the walls of phthisical cavities is aneurysm common. In large peripheral arteries, tuberculous arteritis is rare and consequential aneurysm even rarer. Indeed in 1927, Brockman found few references to tuberculosis affecting large arteries and all those concerned the aorta, involved by direct extension from neighboring lesions. The same author reported a tuberculous aneurysm in a boy, aged 14 years, affecting the right common femoral artery. While there was tuberculous disease of the spine there was no focus in the neighborhood of the affected artery, and Brockman was of the opinion that the infection had been blood borne to the femoral artery; but it appears possible to us that the etiology may well have been the same as in our case, namely, spread of infection via the lymphatic chains from the spinal focus of the disease. The rarity of tuberculosis affecting peripheral limb vessels is further stressed by the fact that it received no mention in a symposium on aneurysm held at the Lisbon Congress of the International Surgical Society in 1953.

From a therapeutic point of view it is interesting to note that surgical intervention can be carried out with repair of arterial trunks in the presence of infection. The success of this procedure is attributed to removal of the infected tissue, full treatment with the appropriate antibiotic and chemotherapeutic agents, and the utilization of anticoagulants.

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DIAPHRAGMATIC HERNIA THROUGH THE FORAMEN OF MORGAGNI

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HERNIATION of intra-abdominal viscera into the chest through the diaphragm has been a known pathologic entity since Paré's description of 2 cases of traumatic hernia in 1579. In a monograph, written in the eighteenth century, Morgagni first described herniation through the retrosternal aspect of the diaphragm. In his cases the diaphragmatic hernia protruded through the anterior part of the diaphragm behind the xiphoid cartilage. This aperture has since become known as the foramen of Morgagni, and protrusions occurring in this region are known as diaphragmatic hernia through the foramen of Morgagni. Various adjectives have also been used to describe these hernias, such as retrosternal, parasternal, substernal, and subcostosternal. These hernias are the least common of the various types of diaphragmatic hernia as evidenced by the relatively small number of cases found in the literature; however, their actual incidence is difficult to determine as many may be asymptomatic and go undiagnosed.

ANATOMY

The origin and attachments of the diaphragm are extensive. Nevertheless, this structure originates essentially from four areas—sternal, costal, crural, and the arcuate ligaments (medial and lateral) as illustrated in Figure 1. The sternal origin, which concerns us most in this discussion, consists of short right and left slips from the posterior aspect of the xiphoid process. These slips are separated from one another by areolar tissue. Their fibers pass upward and backward to insert into the anterior margin of the central tendon.

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Normally there exists in both leaves of the diaphragm a triangular space with its apex pointing toward the central tendon. The space is devoid of muscle fibers and is between the sternal and anterior costal attachments of the diaphragm. It is covered above by pleura and pericardium and below by peritoneum. In the fetus and the infant it is comprised, in part, of disconnected muscle fibers which disappear during adolescence. The superior epigastric vessels and lymphatics traverse this space.

ETIOLOGY

Hernias that penetrate the foramen of Morgagni are direct ones of the acquired type and all are covered by a peritoneal sac. They are infrequently encountered in infants. Two possible explanations have been advanced for this fact: (1) the relatively large size of the liver in early life forms a natural closure to the two parasternal apertures in the diaphragm, and (2) in this age group the transverse mesocolon is relatively short. The presence of fat in the space of Morgagni may play an etiologic role in the development of this hernia. Abundant fat may displace the adjacent muscular tissue, thus enlarging and further weakening an already relatively weak area. Repeated rapid changes in intra-abdominal pressure may constitute the inciting cause for a hernial sac to force itself through the space.

The predominant occurrence of these hernias on the right may be due to the larger attachment of the pericardium to the left side of the thoracic diaphragm. The hernial aperture frequently is unequally divided by the falciform ligament, the medial space being smaller. Occasionally the sternal at-

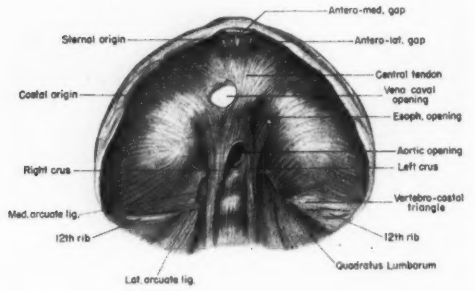


FIG. 1.

FIG. 1. Origin and attachments of the diaphragm. The potential hernia site (anterolateral gap) through the triangular space of Morgagni is illustrated.

FIG. 2. Cross section just above diaphragm viewed from above. This shows relationship of herniation through right and left foramina of Morgagni to the heart and pleural cavities. In large hernias on the left the heart is displaced posteriorly and to the patient's right.

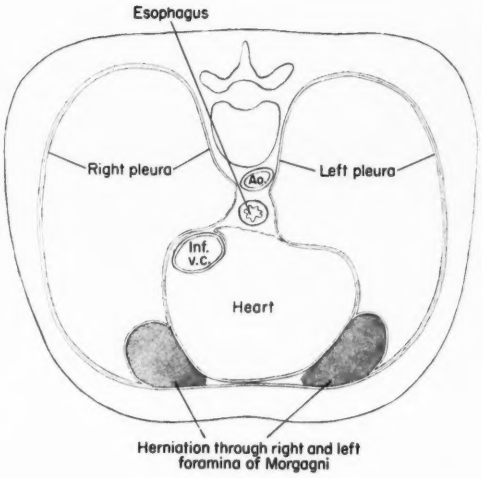


FIG. 2.

tachment of the diaphragm is entirely absent and the two foramina of Morgagni are fused into one large defect behind the sternum and adjacent costochondral junctions. Hernias extending into the right pleural cavity displace the heart to the left; those extending into the left pleural cavity displace the heart posteriorly (Fig. 2). There may be compression of the phrenic and vagus nerves, and the lower pulmonary lobes.

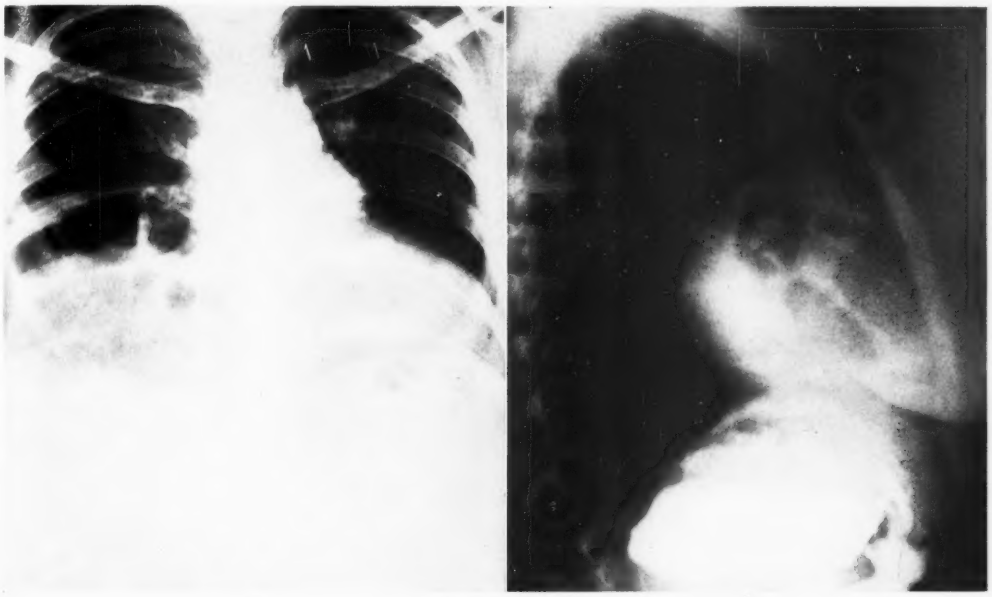
SYMPTOMS

The complex and indefinite associated symptoms may be mild or severe and are produced by the various thoracic and abdominal structures involved in the hernia. Cardiorespiratory symptoms are said to be the most common, although in our experience gastrointestinal complaints predominate. Cough, precordial pain, retrosternal pressure, palpitation, and dyspnea are produced by the mechanical presence of the hernia within the chest. Gastrointestinal symptoms may mimic those of disease of the gallbladder, pancreas, stomach, duodenum, and colon. Irritation of the phrenic nerve endings may account for symptoms frequently ascribed to disease of the gallbladder. The hernial contents are most commonly omentum, transverse colon, and rarely the stomach, liver, and ileocecal junction. Although incarceration is sometimes found, strangulation has been infrequently reported.

DIAGNOSIS

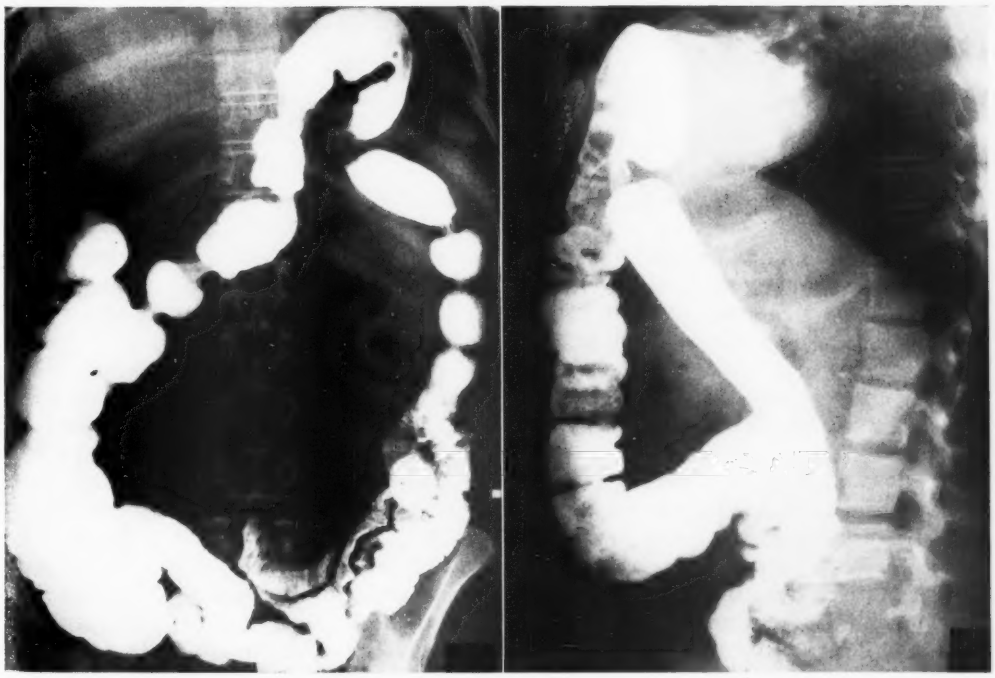
Prior to the advent of the roentgenogram, the great majority of diagnoses were made by the pathologist in unsuspected cases. Waelli in 1912 was the first to report a parasternal hernia diagnosed by roentgen examination, and since then this diagnostic aid has furthered our knowledge of this condition considerably.

The differential diagnosis of masses in the anterior and midportion of the pulmonary field at the cardiophrenic angle involves a consideration of several pathologic entities among which might be mentioned lymphoma, teratoma, lipoma, peripheral pulmonary neoplasms, hydatid disease, empyema, and pleural and pericardial cysts. On roentgen examination (Figs. 3, 4, and 5), hernias through the foramen of Morgagni are characterized by a rounded, soft tissue density in this area. Its borders are usually sharp and well defined, but it cannot, as a rule, be separated from the right border of the heart



a b

FIG. 3.

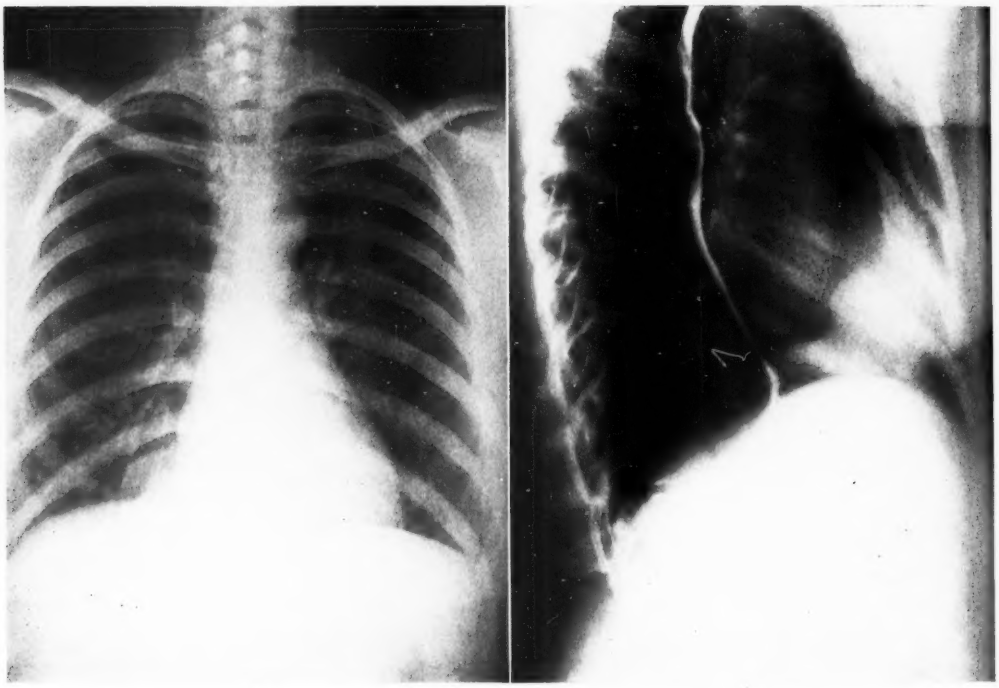


a b

FIG. 4.

FIG. 3. Case 1 (1946). a, Abnormal density suggests intestine in right lower thorax. b, Lateral view shows shadow to be anterior and suggests Morgagni hernia.

FIG. 4. Case 1 (1953). a, Barium enema shows left Morgagni hernia with transverse colon in left chest. b, Left lateral view; the defect is anterior in the diaphragm.



a b

FIG. 5. Case 5. a, A more typical Morgagni hernia than that shown in Figures 3 and 4, illustrating difficulty in differential diagnosis. b, Lateral view showing anterior lesion.

shadow. The mass does not pulsate but may be difficult to distinguish from pericardial cysts even after careful fluoroscopy. There may be basal atelectasis of the adjacent compressed lung. If bowel loops are present within the hernial sac, the intestinal pattern which may be seen is diagnostic, although an erroneous impression of encapsulated pleural fluid may be made if the bowel loop contains fluid levels. Roentgen study of the barium-filled gastrointestinal tract, pneumothorax, and pneumoperitoneum may be helpful diagnostic aids. If the hernial sac contains omentum alone, the correct preoperative diagnosis may not be definite from the roentgen studies; however, in these cases the gas pattern in the large bowel may be seen very high on the lateral roentgen view. Physical examination in these cases produces the findings of any other lower anterior thoracic mass, but if a succussion sound synchronous with the heart action is detected the correct diagnosis may be suspected.

TREATMENT

Surgical reduction and repair of the hernia is usually advisable, either because of associated symptoms or, in some cases, because a preoperative diagnosis cannot be made. We believe that transabdominal repair is preferred. On occasion it is difficult to ascertain preoperatively whether the hernia originates on the right or left side; these areas are both accessible from the abdominal approach. A better closure of the diaphragmatic defect may be possible at times through the abdominal route, although we have not encountered technical difficulty using the right transthoracic approach.

TABLE I.—SUMMARY OF 9 CASES OF MORGAGNI HERNIA IN 8 PATIENTS

Case	*Age and sex*	*Preoperative weight, pounds*	*Location and hernial content*	*Symptoms and duration*	*X-ray findings*	*Preoperative diagnosis*	*Surgical approach*
1*	44 F	160	Right; transverse colon and omentum	Epigastric distress, constipation, 6 years	Diagnosis by barium enema	Morgagni hernia	Transthoracic
2	62 F	135	Right; portions of stomach, transverse colon, and omentum	Flatulence, eructation, vomiting without nausea, heartburn, 2 years	Diagnosis by gastrointestinal series and barium enema	Morgagni hernia	Transthoracic
3	No operation—chest x-ray diagnosis only						
4	52 F	—	Right; omentum	Retrosternal discomfort, 1 year	Mass at right cardiophrenic angle	Intrathoracic tumor	Transthoracic
5	49 F	156	Right; omentum	None	Mass at right cardiophrenic angle; normal barium enema; survey film of chest 12 months previously, negative	? Morgagni hernia ? Pleural cyst	Transthoracic
6	69 F	132	Right; omentum	Epigastric pain, fatigue, weakness, 2½ years	Mass at right cardiophrenic angle	? Morgagni hernia ? Pleural cyst	Transabdominal; patient also had gastric ulcer; concomitant gastrectomy and herniorrhaphy
7	55 M	174	Right; omentum	Fatigue, 2 months	Mass at right cardiophrenic angle; barium enema, negative	Mediastinal tumor	Transthoracic
8	55 F	159	Right; portion of stomach, transverse colon, and omentum	Epigastric distress and flatulence, 9 years	Diagnosis by gastrointestinal series and barium enema; chest film suggestive	Morgagni hernia	Transthoracic
9	54 M	144	Right; omentum compressing right middle lobe	Mild cough, several years	Mass in right lower mediastinum	Mediastinal tumor	Transthoracic

*This patient was operated on 7 years later for repair of left Morgagni hernia by transabdominal approach. Contents of the hernial sac were transverse colon and omentum.

The redundant peritoneal sac should be excised following reduction of the hernia. These maneuvers may be technically difficult when the sac is fused with the pericardium. For small linear openings a simple overlap of the adjacent diaphragmatic margins is all that is necessary. For larger openings the anterior margin of the defect may be sutured to the posterior rectus sheath and anterior thoracic wall. Use of a sliding pedicle flap fashioned from the transversus abdominis muscle has been described to close large midline defects from below. Free, autogenous fascial grafts or fascial sutures may be utilized for repair. In the abdominal approach the round and falciform ligaments may be incorporated in the closure to strengthen it as well as to reattach it to the anterior abdominal wall. Although phrenic nerve crush may render easier closure of the defect, the desire to maintain an adequate pulmonary ventilation immediately after operation would seem to preclude its routine use.

Nine cases of hernia through the foramen of Morgagni have been surgically treated at the Lahey Clinic. From Table I it is apparent that of the 8 patients who were operated on, 6 were women and 2 were men. One patient had 2 operations for a Morgagni hernia. In 8 cases the hernia presented on the right and in 1 on the left. This latter case is of particular interest in that the herniation on the left was known to have developed within 2 years after a transthoracic repair of a right-sided Morgagni hernia.

Most of the patients were obese or somewhat overweight. The preoperative diagnosis was correct in those cases in which there were present herniated abdominal viscera, namely transverse colon or stomach, or both. In those cases in which omentum alone formed the hernial contents the preoperative diagnosis usually was questionable and an intrathoracic tumor was suspected. Transthoracic approach was employed in all these latter cases. Symptoms varied according to hernial content and were usually related to the gastrointestinal tract. No cases of strangulation were encountered.

SUMMARY

Diaphragmatic hernia through the foramen of Morgagni is an acquired herniation occurring most commonly in middle aged patients. These hernias are covered by a peritoneal sac and most often contain omentum, less often portions of the transverse colon, stomach, and liver. They occur predominantly through the right parasternal space. Their development may be related to obesity, degenerative changes, and repeated rapid changes in intra-abdominal pressure. Symptoms encountered are related to mechanical changes in the structures involved. Strangulation of hernial contents rarely occurs. Diagnosis may be difficult if only omentum is involved.

This condition should always be considered in the differential diagnosis of asymptomatic lesions in the lower portion of the chest anteriorly. If the stomach or colon is involved, the diagnosis may be correctly made by barium x-ray studies. Surgical repair may be carried out either through the chest or through the abdomen.

An interesting case of the development of a left-sided Morgagni hernia (Fig. 4) 2 years after repair of a large right-sided hernia (Fig. 3) through the foramen of Morgagni is presented.

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AN ANALYSIS OF ONE HUNDRED AND FIVE RADICAL HYSTERECTOMIES AT THE FREE HOSPITAL FOR WOMEN

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RADICAL HYSTERECTOMY and pelvic lymphadenectomy for invasive carcinoma of the cervix were performed in 105 cases at the Free Hospital for Women between 1943 and 1953 inclusive. This material is of interest because of the relative paucity of reports dealing with the surgical aspects of this disease presented during the last decade. It has been well known, and has recently been reemphasized, that certain cervical cancers respond well to radium and x-ray whereas others respond poorly or not at all. Obviously, the latter patients should be treated surgically. Methods designed to provide early selection of radioresistant cases have been suggested and are being evaluated in several large gynecologic clinics throughout this country and abroad. However, at the present moment the only method of selection is a clinical one, that is, the extent of the disease and the technical ease with which the diseased area may be removed. This report deals only with invasive cancer, all the pathologic material having been reviewed and all cases of carcinoma in situ or "questionable early stromal invasion" removed.

The surgical approach to the treatment of cervical cancer was initiated in the Free Hospital for Women in 1908 and between that time and 1942 eighty-three "radical" hysterectomies were performed. This represented 6.3 per cent of the total number of patients with cervical cancer treated during that interval. While it is not deemed worth while to evaluate these procedures critically at this time, it is interesting to note that 60 of these patients may now be classified in League of Nations stage I and 23 in stage II. Postoperative complications were frequent and included 10 fistulas, 4 patients with peritonitis, 2 with wound dehiscence, and 2 with evisceration. The morbidity rate was 71 per cent. The 5 year survival rate was 40 per cent in stage I and 30 per cent in stage II. Twelve of the 83 patients were found to have positive lymph nodes (14 per cent), and the 5 year survival in this group was 8.3 per cent. Improvements in all of these variables will be noted in the series of patients treated between 1943 and 1953, and it is hoped that by optimum selection the continued rate of improvement in surgical treatment will be materially accelerated.

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SELECTION OF PATIENT FOR OPERATION

The majority of patients treated by radical hysterectomy were classified as stage I preoperatively, and it is obvious that, if this staging is correct, the best results will occur in this group. This observation will be considered in detail in the analysis of results but, in general, it should be stated that careful preoperative examination and study are mandatory if this extensive surgery is contemplated. Stage III and stage IV patients are not suitable since adequate dissection beyond the boundaries of tumor is not technically possible. One may also assume that surgical manipulation in such patients (short of pelvic evisceration) may actually disseminate tumor cells by vascular and lymphatic channels.

League of Nations stage II has been divided into subgroups A and B, the suffix A implying spread beyond the cervix onto the vagina but not farther than the upper third. The suffix B connotes lateral paracervical,

TABLE I.—MEDICAL ILLNESSES PRIOR TO RADICAL HYSTERECTOMY

	No. of cases
Hypertension	19
Pneumonia	8
Rheumatic fever	3
Diabetes	2
Pleurisy	2
Typhoid fever	2
Diphtheria	2
Peptic ulcers	2
Pyelitis, recurrent	2
Pulmonary tuberculosis	2
Poliomyelitis	1
Ulcerative colitis	1
Pernicious anemia	1
Chronic nephritis	1
Pelvic inflammatory disease	1
Influenza	1
Rheumatic heart disease	1
Syphilis	1

parametrial, or paravaginal involvement but not extending to the lateral pelvic wall. Results should be evaluated separately since it is obvious that prognosis in stage IIB is poorer than in stage IIA. Frequently, however, the examiner interprets inflammatory processes or scarring from endometriosis as tumor and is pleasantly surprised when the true extent of carcinoma is evident at surgery. Thus stage IIB or even stage III, while permanently coded as such, must then be considered to be a postoperative stage I and evaluated accordingly. In the analyses this postoperative surgical and pathologic classification has been utilized in addition to the usual preoperative one suggested by the League of Nations.

The stage of carcinoma should not be the only factor in selection for radical hysterectomy. The general status of the patient must be carefully evaluated together with investigation of cardiac, pulmonary, and renal systems. Obesity is a major factor in selection since it makes dissection in the deep recesses of the pelvis difficult and incomplete. Furthermore, postoperative complications in this group are increased. The surgical approach in such patients, if surgery is indicated at all, may be by the vaginal method popularized by Schauta and recently by Navatril.

Compensated heart disease, regulated diabetes, anemia, and old age are not, per se, contraindications to radical surgery. Complete medical evaluation prior to surgery will prevent anesthetic, surgical, and immediate postoperative accidents.

PREOPERATIVE STUDY AND PREPARATION

In an effort to minimize postoperative morbidity and prevent mortality a thorough investigation of all major systems is indicated. The frequency of involvement of the urinary tract warrants complete evaluation which should include cystoscopy, intravenous pyelography, determination of blood nonprotein nitrogen, and routine urinalyses and cultures if indicated. The rectum and lower sigmoid should be carefully visualized by proctosigmoidoscopy. A roentgenogram of the chest is routinely performed and the cardiovascular potential determined. Electrocardiograms are performed on all patients over the age of 50 years. A "metastatic series" of roentgenograms should be done to rule out involvement of skull, vertebrae, and long bones by tumor.

Blood chemistries and hematologic profile should be carried out in order to secure a baseline for later replacement therapy and also for the correction of preoperative deficits. A basic minimum should include a complete blood count, hematocrit, serum sodium, potassium, chloride, and nonprotein nitrogen. Many clinics are now equipped to perform blood volume estimations which offers an additional preoperative safeguard.

If varicose veins are prominent or if there has been a history of previous phlebothrombosis or thrombophlebitis, both legs are wrapped snugly from ankle to mid-thigh with ace bandages. Preliminary femoral ligation has not been performed but prophylactic dicumarol is given routinely. If the patient weighs over 140 pounds, 200 milligrams are given the evening prior to surgery; if under 140 pounds the dose is 100 milligrams. Therapy is continued by giving 100 milligrams every 4 days as long as the patient is hospitalized.

Intestinal decompression has been used in selected cases but not routinely. If it is de-

cided upon, a Cantor or Miller-Abbott tube is inserted the afternoon prior to surgery and the patient is then permitted to be ambulatory, consequently aiding in the descent of the tube.

Penicillin and streptomycin are started the day prior to surgery, and the diet is restricted to liquids during the immediate preoperative phase.

THE ANALYSES

One hundred and five cases of carcinoma of the uterine cervix treated surgically between 1943 and 1953 inclusive have been analyzed. The oldest patient in the group was 70 years old, the youngest 25 with an average age of 42.9 years. This average age is 10 years younger than that found when radical hysterectomies were done for endometrial cancer. The age range was: 6 patients between 20 and 30 years old; 32 between 30 and 40; 44 between 40 and 50, 16 between 50 and 60; 5 between 60 and 70; and 1 over 70 years old.

Race. One hundred and four patients were white and 1 was colored. Two Jewish women, both married to Jews, were treated. Both husbands had been circumcised.

Family history of carcinoma. Carcinoma occurring in the patient's immediate family (mother, father, siblings) was noted in 13 cases. These included 3 patients with breast cancer, 2 unspecified, and 1 each involving stomach, mouth, throat, testicle, liver, brain, bladder, and blood.

Weight. Although obesity has been previously mentioned as a serious obstacle to the performance of an adequate operation, 26 patients in this series weighed over 150 pounds. However, this must be evaluated in regard to the general body habitus, height, and areas of fat deposition. The heaviest patient weighed 196 pounds and 74 weighed between 100 and 149 pounds. Five weighed less than 100 pounds with the lightest scaling 86 pounds. The average weight was 135 pounds as compared with an average of 150 for radical hysterectomies performed for endometrial carcinoma.

TABLE II.—SURGICAL PROCEDURES PRIOR TO RADICAL HYSTERECTOMY

	No. of cases
Appendectomy	19
Unilateral oophorectomy	13
Ectopic pregnancy	3
Supravaginal hysterectomy	4
Cesarean section	3
Bilateral salpingo-oophorectomy	3
Bilateral tubal ligation	2
Myomectomy and unilateral salpingo-oophorectomy	2
Cholecystectomy	2
Uterine fundectomy and bilateral salpingo-oophorectomy	1
Unilateral salpingo-oophorectomy and ligation of opposite tube	1
Simple mastectomy	1
Anterior suspension and colporrhaphy	1
Repair rectovaginal fistula	1
Thyroidectomy	1
Herniorrhaphy	1

Medical history. Almost every serious medical illness is included in the list obtained from the past history of the 105 patients undergoing radical surgery. As evident in Table I, cardiac, gastroenterologic, pulmonary, and urinary systems have representative illnesses of major severity. Five patients had systolic blood pressures of over 200, 1 had had previous cardiac failure, and 1 had a history of myocardial infarction. All did well postoperatively.

Surgical history. Table II lists the various surgical procedures that had been performed prior to radical hysterectomy. In 6 patients operations had been performed which resulted in the retention of a functionless uterus (if its sole function is believed to be childbearing). These included bilateral salpingo-oophorectomy in 3 patients, bilateral tubal ligation, 2 patients, and unilateral salpingo-oophorectomy and ligation of opposite tube, 1 patient. In addition, 5 patients had supravaginal hysterectomies and developed carcinoma of the cervical stump. Thus 11 patients would have been spared cancer if more radical surgery had been performed initially.

Marriage. One hundred and one patients were, or had previously been, married and 4 were single. Of the married group, 13 patients had been married twice and 1 had been married 3 times. In addition, 10 patients were divorced but did not remarry.

TABLE III.

L. of N. stage	*No. of patients*	*Postoperative class*	*Correct*	*Understaged*	*Overstaged*
I	85	A	50		
		Ao	22		
		B		2	
		C		1	
		D		8	
		F		2	
IIA	17	A	5		
		Ao	4		
		B	2		
		C		1	
		D		5	
IIB	3	A			1
		Ao			1
		D		1	

Previous studies of the relationship of marriage, marriage under age 20, and the importance of multiple sexual partners have been published within the last few years, and all seem etiologically related to cervical cancer.

Parity. Eleven of the 101 married patients had not conceived. Seventy-three patients had had from 1 to 4 term deliveries and 17 patients had over 4. The greatest parity recorded was 11, occurring in 2 patients. The average parity of the married patients was 2.6. By comparison, in the patients who had radical hysterectomies for endometrial cancer the average parity was 1.6. In our series of patients with carcinoma of the cervix complicating pregnancy the average parity was 4.9.

Age at marriage. The average age at the time of marriage of the 101 married patients was 22.0 years, the youngest being 14 and the oldest 45. Forty-four patients (43.5 per cent) were married before their twentieth birthday, 54 were married between age 20 and 39, and 3 were married after they had attained the age of 40. In previous studies by Lombard and Morris and their associates, marriage before the age of 20 years has been found to be statistically correlated and etiologically related to the development of cervical cancer. In Lombard and Potter's study, 44.6 per cent (as compared with 23.7 per cent of matched controls) were married before the age of 20. In addition, they found marriage at any age to be significant in relation to cervical cancer.

The average age at marriage of the patients in the endometrial carcinoma group treated by radical hysterectomy was 26.0 years.

Stage of disease. Utilizing the League of Nations classification for preoperative classification, 85 patients were placed in stage I, 17 patients in stage IIA, and 3 patients in stage IIB.

The pathologic and surgical (postoperative) classification suggested by Meigs and Liu (12) has been employed to give a more detailed and correct analysis of the extent of tumor. This classification is as follows:

Class O: Carcinoma in situ, also known as preinvasive carcinoma, intraepithelial carcinoma, or microcarcinoma.

Class A: Carcinoma confined strictly to the cervix.

Class Ao: No tumor in the cervix in the surgical specimen after a positive biopsy of infiltrating carcinoma.

Class B: Carcinoma extending from the cervix to involve the vagina except for the lower third. The carcinoma extends into the corpus and may involve the upper vagina and corpus. Vaginal or uterine extension may be by direct spread or by metastasis.

Class C: Carcinoma involving paracervical or paravaginal tissue by direct extension or by lymphatic vessels or in nodes within such tissue. Spread may be by vaginal metastasis or by direct extension into the lower third of the vagina.

Class D: Lymph vessels and node involvement beyond paracervical and paravaginal regions, including all lymph vessels or nodes in the true pelvis, except as described in class C. Metastases occur to ovary or tube.

Class E: Carcinoma that has penetrated to the serosa, musculature, or mucosa of the bladder, or to the colon or rectum.

Class F: Carcinoma involving the pelvic wall or aortic nodes.

The errors of clinical (League of Nations) staging are evident by review of Table III. It is evident that of the 85 patients in stage I (League of Nations) 72 were correctly classified. Actually 22 patients were placed into Class Ao, that is, they had no tumor in the excised specimen. This, it may be assumed, was due to marked radiosensitivity of the tumor (all were given preliminary radium), removal of all the tumor by the original biopsy (not likely), or incomplete pathologic study. However, as will be seen later, all of

these patients are surviving at the present time so that the last assumption is probably not valid. Two patients had tumor in the vagina microscopically and therefore were classed as B. (They should have been IIA, League of Nations.) One patient had tumor in a single parametrial lymph node (class C), and 8 patients had spread to obturator and/or iliac nodes (class D). Two patients had carcinoma involving the aortic nodes (class F). Lymph node metastases were therefore present in 11 of 85 patients originally placed in stage I (13 per cent).

In stage IIA, 11 patients were correctly classified and 6 had nodal involvement (35 per cent).

In stage IIB, 2 patients were actually overstaged, since there was no residual tumor in 1 patient and in the other it was limited to the cervix. The third patient had pelvic lymph node metastases and was incorrectly staged.

Thus of the 105 patients, 88 had disease limited to the cervix or no tumor at all in the excised specimen. Seventeen patients (16.1 per cent) had spread to pelvic or aortic nodes.

Histologic grade. Previous studies by our group and by Warren and associates have indicated that the gradation of tumor (histologically) does not accurately prognosticate the survival rate. In a series of 100 cases studied by Kistner and Hertig, grade 2 occurred most often (77 per cent) but was not directly correlated with clinical staging. In this present series of surgically treated cases selection for operation was made without regard for the histology of the tumor.

Seventy-four of the patients had grade 2 carcinomas, 20 had grade 3, 5 had adenosquamous, 3 had grade 1, 2 were not graded, and 1 had adenocarcinoma.

Preoperative radium. Radium was administered preoperatively to 74 patients with the hope that implantation of tumor cells at the time of surgery would be diminished. It was given with standard intrauterine tandem and vaginal "pillbox" after the method devised by G. V. Smith in a usual dose of 3,000 milligram hours. It was administered 1 to 3 weeks prior to surgery.

TABLE IV.—POSTOPERATIVE FISTULAS

Type	*No.*	*Results*	*No.*
Ureterovaginal	5	Spontaneous closure	2
		Repair—good result	1
		Died—carcinomatosis 34 days postop.	1
		Died—pyelonephritis 70 days postop.	1*
Vesicovaginal	4	Repair—good result	3
		Died—pyelonephritis	1*
Rectovaginal	1	Died—pyelonephritis	1*

*Same patient with 3 fistulas.

Twenty-seven of these 74 patients had no residual tumor in the cervix at the time of hysterectomy—all are living without apparent disease 4 to 8 years postoperatively. The details of 5 year survival will be considered under that general heading.

Preoperative vaginal preparation. Routine cleansing of the vagina with aequeous and tincture of zephiran was utilized in all cases, followed (in most of the later cases) by painting the cervix and vagina with Schiller's solution to determine the possible extent of surface tumor or carcinoma in situ. Beginning in 1946, 20 per cent silver nitrate solution was swabbed over the cervix and vagina —again with the idea of diminishing the vitality of spilled tumor cells. Sixty-eight patients were so treated.

Operative technique. The operative technique has been completely presented by several authors in recent years, and the technique used at the Free Hospital is, with minor variations, the same as described by Meigs (10) in his text. One exception has been the ligation of the hypogastric arteries bilaterally just below the level of the superior gluteal and the ureteral branch. Occasionally to prevent embolism the hypogastric veins have also been ligated. Arterial ligation was performed on 17 patients without apparent damage to the bladder or bowel. No fistulas occurred in these patients.

Technical errors. The operation is tedious and, in obese patients, extremely difficult. Technical errors are, therefore, common and somewhat excusable. In this series the bladder was entered 3 times but in each case the

TABLE V.—FIVE YEAR SURVIVORS WITH POSITIVE NODES

Name	*Survival† yrs.*	*mos.*	*Preoperative radium*	*Postoperative x-ray*	*Site of and No. positive nodes*
D. B.	10	6	No	Yes	Not stated
J. N.	8	7	No	Yes	Left hypogastric, right iliac, bifurcation (2)
R. McL.	7	6	No	Yes	Left hypogastric, right hypogastric (2)
M. M.*	5	3	Yes	Yes	Right obturator (1)
A. B.	5		Yes	Yes	Left parametrium, right parametrium (2)

*Now has recurrence in bladder.
†As of September 1, 1956.

defect was recognized, sutured, and no ill effects followed. In 1 of the early operations (Patient 4) in 1945, the right obturator nerve was severed and resutured. There was, however, permanent diminution in adduction of the involved thigh. In 1 patient the left external iliac vein was nicked and ligated without sequelae. The mucosa of the rectum was entered twice but was sutured in each case and no complications were noted.

Operative mortality. One patient did not leave the hospital following surgery and died on the seventieth postoperative day. This constituted the only operative death in the series and actually it was the first one performed—on June 7, 1943.

Mrs. I. V., a 51 year old white female, para 5, was treated with 6,000 roentgens of x-ray and then 5,000 milligram hours of radium beginning on February 28, 1942, for a stage IIA cervical cancer. On August 16, 1942, an additional 2,750 milligram hours of radium were given because of vaginal recurrence. Radium was again administered in April 1943 and May 1943 for persistence of disease. When this therapy was unsuccessful a radical hysterectomy and bilateral pelvic lymphadectomy were performed. The pathologic specimen showed active cancer in the cervix with *no* radiation effect. The uterus also contained tumor as did both parametrial areas but the lymph nodes were negative. There was marked radiation reaction in both parametria.

On the twelfth postoperative day a rectovaginal fistula developed followed by left ureteral obstruction for which a nephrostomy was done. The patient subsequently developed right ureterovaginal and vesicovaginal fistulas. She died on the seventieth postoperative day of chronic pyelonephritis.

This tumor was obviously radioresistant, and surgery was indicated at the time of the first recurrence (probably persistence). It is entirely possible that the fistulas would have developed following the extreme dosage of radium even without surgery but their appearance was hastened by it. Death was caused by damage to the urinary tract, not by extensive cancer.

PATHOLOGY OF EXCISED SPECIMENS

Cervix. As previously noted, 27 of the 105 specimens had no residual tumor at the time of extirpation. All patients had received +3,000 milligram hours of radium. Forty-seven patients (also radium treated) had residual tumor in the cervix with varying degrees of radiation reaction. The remaining 31 patients all had active carcinoma in the specimen.

Uterus. The following findings were noted: Postradiation atrophic endometrium in 32 cases, leiomyomas in 15, adenomyosis in 10, endometrial polyp in 9, senescent endometrium in 8, chronic endometritis in 6, cystic hyperplasia in 5, squamous cell carcinoma—endometrium in 4, anaplasia of endometrium in 3, adenoacanthoma endometrium in 1, placental site (30 days postpartum) in 1, and pregnancy (26 day gestation) in 1 instance.

Ovaries. The following findings were noted: senescent or atrophic ovaries in 29 cases, peri-oophoritis in 21, cortical stromal hyperplasia in 14, cortical fibrosis in 9, endometriosis in 7, follicular cysts in 3, pseudodecidual reaction in 3, adrenal cortical rests in 2, pseudomucinous cystadenoma in 1, metastatic squamous cell carcinoma in 1, Brenner tumor in 1, dermoid cyst in 1, cystadenofibroma in 1, fibroma in 1, and thecomatosis in 1 case.

Oviduct. The following findings were noted: chronic salpingitis in 32 cases, senescence in 15, acute salpingitis in 3, hydrosalpinx in 3, hematosalpinx in 2, perisalpingitis in 2, metastatic squamous cell carcinoma in 1, and menstrual salpingitis in 1 case.

Morbidity and complications. By utilizing the criterion of temperature elevation over 100.4

on any 2 consecutive postoperative days, exclusive of the first 24 hours, 44 of the 105 patients were classified as morbid.

The average hospital stay was 15.2 days with the longest being 52 days and the shortest 8 days.

The list of complications is as follows: bladder atony in 33 cases; pyelonephritis in 12; pelvic hematoma or abscess in 9; ureterovaginal fistulas in 5; vesicovaginal fistulas in 4; rectovaginal fistula in 1; wound sepsis in 6; hydroureter and hydronephrosis in 5; serum collection in pelvis in 4; postoperative ileus (severe) in 3; small bowel obstruction in 2; phlebitis in 2; nonfatal pulmonary embolus in 1; shock (protracted) in 2; atelectasis in 1; wound dehiscence in 1; difficult abduction of leg in 2; diabetic acidosis in 1; nephrostomy in 1; ureteral calculus and obstructed ureter in 1; no kidney function (unilateral) on intravenous pyelogram postoperatively in 1; and heart failure in 1 case.

Any surgeon contemplating this operative procedure should be aware of these complications and should be competent to cope with them should they develop. It is evident that the urinary tract is the system most frequently involved in serious difficulty.

POSTOPERATIVE FISTULAS

Eight patients (7.6 per cent) developed vaginal fistulas and 1 of these (the first patient operated on) had 3 types—ureterovaginal, vesicovaginal, and rectovaginal. She died on the seventieth postoperative day of pyelonephritis. The various fistulas and their outcome are shown in Table IV.

FIVE YEAR SURVIVAL

This most important aspect of the problem will be considered from 3 aspects, the presence of tumor in lymph nodes, the effect of preoperative radium, and the prognostic accuracy of postoperative staging.

Lymph node involvement. Positive lymph nodes were found in 17 patients (16.1 per cent). Five of these are living 5 years subsequent to surgery but 1 has a recurrence. The survivals are for a period of 10 years 6 months, 8 years 7 months, 7 years 6 months, 5 years 3 months, and 5 years respectively as of September 1, 1956. Three patients are living without apparent disease after 4 years 7 months, 2 years 11 months, and 2 years 10 months; and 1 patient is living with a vaginal recurrence at 2 years 2 months. Eight have died of cervical cancer or of complications of surgery.

TABLE VI.—LESS THAN 5 YEAR SURVIVORS WITH POSITIVE NODES

Name	*Survival† yrs.*	*mos.*	*Preoperative radium*	*Postoperative x-ray*	*Site of and No. positive nodes*
M. B.	4	7	Yes	Yes	Right obturator (1)
A. W.	2	11	Yes	Yes	Left hypogastric (2)
H. B.‡	2	10	Yes	Yes	Broad ligament adjacent to ovary (1)
G. O.*	2	2	No	Yes	Left obturator (2)

*Now has vaginal recurrence and rectovaginal fistula subsequent to supervoltage therapy and postoperative radium.
†As of September 1, 1956.
‡This patient received x-ray as well as radium prior to surgery.

Table V outlines the data on the five 5 year survivors with positive nodes. Only 2 of the 5 had preoperative radium, and the nodes involved in these patients were the right obturator in one and parametrial nodes in the other. One of these (M. M.) has bladder recurrence at the present time. No evidence of radiation reaction was seen in the lymph nodes obtained in these 2 specimens. It is interesting to note, however, that all surviving patients had postoperative x-ray therapy, whereas of the 8 patients with positive nodes who are now dead only 4 received postoperative x-ray therapy.

Table VI outlines the data on the 4 less than 5 year survivors with positive nodes. It is evident here also that all patients received x-ray therapy, 3 postoperatively (when the radiologist knew the exact site of the involved nodes) and 1 preoperatively. Again, there was no evidence of radiation reaction in the lymph nodes in the 1 patient who received both radium and x-ray before surgery. One patient did not receive preoperative radium because of a poor sensitivity response (part of a Graham study) but did receive postoperative x-ray when it was found that she had positive left obturator nodes. Ironically she is the only patient with recurrence (vaginal) in this group. One can only

TABLE VII.—MORTALITY IN PATIENTS WITH POSITIVE NODES

Name	*Died*	*Preoperative radium*	*X-ray*	*Site of and No. of nodes*	*Cause of death*
I.V.	70 days	Yes*	Yes (preop.)	Both parametia (?)	Pyelonephritis (autopsy)
I.L.	1 yr. 8 mo.	No	No	Preaortic, ext. iliacs (2)	Carcinomatosis (autopsy)
A.R.	34 days	No	No	Not stated	Cardiac failure and diabetes (no autopsy)
M.C.	4 yr. 6 mo.	Yes*	Yes (preop.)	Left hypogastric (1)	Recurrent carcinoma (no autopsy)
C.C.	2 yr. 6 mo.	Yes	Yes (postop.)	Hypogastric (3)	Recurrent carcinoma (no autopsy)
M.C.	8 mo.	Yes	Yes (postop.)	Rt. obturator, rt. ext. iliac, left parametrium (3)	Uremia, carcinomatosis (no autopsy)
L.K.	2 yrs.	No	Yes (postop.)	Both parametria (?)	Recurrent carcinoma (no autopsy)
R.C.	3 yr. 2 mo.	Yes	No	Left obturator, left hypogastric (5)	Uremia, recurrent carcinoma (no autopsy)

8 of 17 patients died.
*Radium here given preoperatively with x-ray as primary treatment. Surgery carried out for radiation failure.

speculate as to whether preoperative radium might have prevented this recurrence.

Table VII outlines the method of therapy, site and number of involved pelvic nodes, and cause of death in the 8 patients now dead. One patient (I. V.) died on the seventieth postoperative day of pyelonephritis and ureteral obstruction. Another died of cardiac failure and diabetes on the thirty-fourth postoperative day. The remaining 6 patients all died of recurrent carcinomatosis in periods varying from 8 months to 4 years 6 months. Five of the 8 patients received preoperative radium but in 2 of these it was given, along with preoperative x-ray, as primary treatment, and surgery was then carried out for radiation failure. In neither of these cases did the involved nodes show radiation reaction. Three patients received postoperative x-ray therapy and 3, for reasons unknown, did not.

The hypogastric nodes were involved in 3 patients, obturators in 2, external iliacs in 2, and preaortic in one. In 2 patients the only nodes involved were in the parametrium.

Eighty-eight patients (83.9 per cent) had negative nodes. Thirty-five are living without apparent disease for over 5 years, 43 are living without apparent disease for from 3 to 5 years, and 1 patient is living with disease. Nine patients who had negative nodes but who had residual tumor in the cervix at the time of surgery are dead. Seven died of extension of their disease, 1 developed a second primary (lung) tumor, and 1 committed suicide.

Table VIII summarizes the survival in relation to the lymph node findings.

Preliminary radium. Seventy-four patients had radium administered to the cervix, uterus, and vagina preoperatively. Of these 74: (1) 27 had no residual tumor in specimen with negative nodes (all living without apparent disease); (2) 38 had residual tumor in specimen and are living without apparent disease (4 of these had positive nodes); (3) 9 had residual tumor in specimen and are dead (5 of these had positive nodes, 3 had negative nodes yet died from spread of cancer, 1 patient with negative nodes died from alcoholism).

Thirty-one patients did not receive preoperative radium. Of these 31: (1) all had residual tumor in specimen; (2) 8 had positive lymph nodes—3 are dead; (3) 23 had negative lymph nodes—5 are dead.

Thus the incidence of positive nodes was 12 per cent with an 88 per cent survival with preliminary radium whereas without radium the incidence of positive nodes was 25.8 per cent with a 74.2 per cent survival (2 plus years).

It should be noted that the decision as to whether radium would be given preopera-

tively was not always based on the size of the lesion or the clinical staging. Some members of the staff, in an effort to determine the potential of surgery alone, elected not to add another variable. Also of interest is the fact that the 105 radical hysterectomies analyzed here were performed by 16 different surgeons, 8 of these during their residency training. The majority, however, were performed by 3 members of the senior staff. This is in contrast to other series in which one surgeon has been the sole operator.

Survival correlated with postoperative staging. Tables IX, X, and XI outline the results of survival if the spread of disease is determined by study of the excised specimen. Thus in stage I (Table IX) it is evident that in the 22 patients who *did not* have residual tumor in the cervix (Ao), survival was 100 per cent. In the 50 patients who *did* have residual tumor but negative nodes (class A), 7 deaths occurred. Two had pelvic recurrence, 3 had distant metastases, 1 developed a second primary, and 1 committed suicide. In the 2 instances in which spread had occurred to the fundus or upper vagina, both patients are surviving (class B). The 1 patient who had a solitary parametrial lymph node (class C) is living without apparent disease after more than 5 years. Eight patients (of stage I) had distant pelvic node involvement (class D), and 4 of these died of recurrence or uremia in less than 5 years whereas 4 are living for over 5 years. The 2 patients who had aortic node involvement (class F) died in less than 2 years.

Patients in stage IIA show similar results (Table X). Thus of 9 patients in class A or Ao, all are living without apparent disease. In class B, 1 patient died 3 years and 7 months postoperatively of recurrence. It is probable that the line of surgical excision in the vagina was not wide enough. This patient did not receive preliminary radium. One patient in class C (spread to parametrium but negative nodes) died 70 days postoperatively of ureteral obstruction, and of the 5 patients in class D, 2 are living without apparent disease (after 2 years 11 months and 2 years 10 months), and 2 have recurrence. One patient in class D died 3 years 11 months postoperatively of uremia and recurrence.

TABLE VIII.—SURVIVAL IN RELATION TO LYMPH NODES

	Positive nodes	*Negative nodes*
Living 5 years and without disease	4	35
Living 3–5 years without disease	3	43
Living with disease	2	1
Dead	8	9
Total: No.	17	88
Per cent	16.1	83.9
Survival (2 years or more), per cent	53	89.8

In stage IIB (Table XI), class A and Ao patients are living without apparent disease whereas the patient in class D died 34 days postoperatively of carcinomatosis and diabetes.

DISCUSSION

In an evaluation of his first 100 radical hysterectomies Meigs (9), in 1953, concluded: "(1) Some patients with positive nodes can be cured by surgical means for 5 years. (2) Local recurrence is less likely following surgical excision than following radiation therapy. (3) There is a suggestion . . . that heavy treatments with radiation are not necessary to cure the local disease and that radiation as given is not likely to destroy tumor in lymph nodes. (4) Except in patients with positive nodes, a cure of the local disease can be expected."

These statements, if analyzed critically, mean that if a patient with cervical cancer has positive lymph nodes, radiation cannot cure her and surgery offers only a slightly better chance. (Meigs reported that only 5 patients of 66 with positive nodes in stage I, and 1 patient of 34 with positive nodes in stage II were living 5 years at the time of this report). What, then, is gained by the radical hysterectomy and particularly by the pelvic lymphadenectomy beyond improved staging of disease and more accurate prognosis? If the tumor is confined to the cervix would not the results be comparable if only a wide resection of the diseased area (without lymphadenectomy) was carried out? The

TABLE IX.—SURVIVAL IN STAGE I ACCORDING TO POSTOPERATIVE STAGING

Class	*No. of patients*	*No. of deaths*	*Comments*
A	50	7	1 died after 3 yrs. 6 mos., chest metastases 1 died after 1 yr. 3 mos., chest metastases 1 died after 1 yr. 6 mos., pelvic recurrence 1 died after 1 yr. 7 mos., cerebral metastases (removed cervix showed lymphatic permeation) 1 died after 5 yrs. 11 mos., 2nd primary bronchogenic carcinoma 1 died after 2 yrs. 5 mos., pelvic recurrence (pelvic delivery 1 mo. prior to treatment) 1 died after 4 yrs. 5 mos., suicide, no tumor
Ao	22	0	—
B	2	0	Both living and well over 5 yrs. (These are really L. of N. stage IIA.)
C	1	0	Living and well 5 yrs.
D	8	4	1 died after 2 yrs. 6 mos., recurrence, positive iliac nodes 1 died after 8 mos., uremia and carcinomatosis, positive iliac nodes 1 died after 2 yrs., pelvic recurrence, positive obturator nodes 1 died after 4 yrs. 6 mos., recurrence, positive iliac and obturator nodes 1 living 10 yrs. 6 mos., positive nodes (site unknown) 1 living 8 yrs. 7 mos., positive hypogastric and iliac nodes 1 living 7 yrs. 6 mos., positive hypogastric nodes 1 living 5 yrs., positive parametrial nodes
F	2	2	1 died after 1 yr. 8 mos., carcinomatosis 1 died after 1 yr. 5 mos., carcinomatosis

effectiveness of the operation seems to be correlated with the thoroughness with which the actual tumor (in cervix, uterus, vagina, and parametria) is removed. In many cases the same result can be effected by radiation; in others, radioresistant, surgery is necessary.

The tenets quoted, however, are not uniformly accepted, and conflicting evidence regarding the curability of regional lymph node metastases in cervical cancer has been presented. Morton first called attention to the fact that, in his series, patients who received x-ray preoperatively had positive nodes less frequently than those who did not. The findings in this series are similar with preliminary radium although the figures are too small to be significant and one wonders about the amount of gamma roentgens delivered by a half-dose of radium to obturator and iliac nodes. Gorton found the very low incidence of 10 per cent nodal involvement in stage I cases after radiation and 18 per cent in stage II. These tumors, however, had responded well locally. (In our series the incidence of positive nodes was 12 per cent in both stage I and II patients after radiation and 25.8 per cent without radiation.) Conversely, Cherry and co-workers found an abnormally high incidence of nodal involvement (34 per cent in stage I and 51 per cent in stage II) after radiation therapy but here radical surgery was performed only on those patients whose local tumor responded poorly to radiotherapy.

The logical conclusions to draw from these data are: (1) that the incidence of lymph node metastases is higher in radioresistant tumors; (2) that properly directed radiation can kill cancer in pelvic nodes (it is perhaps true that metastases from radiosensitive cancers are radiosensitive too), and (3) that in certain cases, after cure of the primary cancer, pelvic metastases will spontaneously regress.

Certain generalizations may, therefore, be made concerning lymph node metastases. Combined statistics of many series show that 15 per cent of patients with stage I lesions, 27 per cent with stage II, and 66 per cent with stage III will have positive nodes at the time of surgery. Furthermore, in a combined group of 1,369 patients reported by Graham, 404 had positive nodes, and of these 21 per cent were living and well at 5 years. Sixty-two per cent of the 965 patients with negative nodes survived 5 years. If preliminary radium is given to radiosensitive tumors, local regression may be expected, and in addition a therapeutic effect upon metastatic nodes is likely. If the cancer is radioresistant (or perhaps the host "cancer sensitive") both local and metastatic sites may be expected to show minimal effect from radiation and probably also from surgery.

The cases discussed in this report represent only 19.4 per cent of the total number of cancers of the cervix treated in this institution during the 11 year interval 1943 to

1953. The remainder were treated by radium and x-ray. Meigs has recently noted, in reporting on the interval from 1942 to 1949, that surgery was used in 22.1 per cent of 622 patients treated at the Massachusetts General and Pondville Hospitals. The over-all 5 year salvage in his group (radiation and surgery) was 45 per cent. Horne has recently reported the latest 5 year study from the Free Hospital for Women (1944 to 1948) in which 270 cases were analyzed. The 5 year survival (radiation and surgery) was 48.5 per cent. Smith's analysis of a previous 5 year interval (1934 to 1938) showed the over-all 5 year survival to be 43 per cent, whereas in the period from 1929 to 1933 it was 38 per cent and from 1914 to 1918 it was 19 per cent.

McDuff has recently presented data from the Rhode Island Hospital (utilizing interstitial needle technique) showing a gradual rise of 5 year survival from 36 to 46 per cent in the last 20 years but no increase in the last 5 year analysis over the previous one. He hopes to improve this by using surgery in selected cases.

Meigs (11), in his most recent article, has partially changed his viewpoint on combinations of surgery and radiation. To quote: "I still have a definite fear of the combination of *full* radiation and surgical extirpation, but from my results it looks as though moderate radiation may be safe . . . I cannot advocate the combination." In his series 12 patients received full radium and full x-ray treatment before surgery and only 6 (50 per cent) lived 5 years. Yet in his analysis by groups he shows 20 patients who had surgery following radiation and no tumor was found in the excised specimen. Nineteen (95 per cent) of these patients survived 5 years and are analogous to our 27 patients with the same treatment. Meigs also shows 29 patients who had surgery after radiation but these are classified as "radiation failures." Five year survival here was 62 per cent. Whether this was "planned preoperative radium" or whether surgery was substituted after radioresistance was found is not stated. Meigs does state, however, that patients who had planned preoperative radiation had the smallest percentage (16.3 per cent) of positive lymph nodes.

Kelso has recently reported 5 year follow up statistics on 89 "unselected" patients with stage I and stage II cervical cancer. He did not use preoperative radium but gave x-ray therapy routinely postoperatively. In stage I, 86.6 per cent survived 5 years (without apparent disease) and in stage II, 68.9 per cent survived (combined 80.8 per cent). Kelso found positive nodes in 15 patients and 60 per cent of these are apparent 5 year cures.

TABLE X.—SURVIVAL OF STAGE IIA ACCORDING TO POSTOPERATIVE STAGING

Class	*No. of patients*	*Comments*
A	5	All living and well
Ao	4	All living and well
B	2	1 living and well 2 yrs. 1 died 3 yrs. 7 mos. of recurrence
C	1	Died 70 days postoperatively of ureteral obstruction
D	5	1 died after 3 yrs. 11 mos., recurrence, uremia 1 living with disease after 5 yrs. 3 mos. (positive obturator) 1 living with disease after 2 yrs. 2 mos. (positive obturator nodes) 1 living without disease after 2 yrs. 11 mos. (positive hypogastric nodes) 1 living without disease after 2 yrs. 10 mos. (metastatic to ovary)

TABLE XI.—SURVIVAL IN STAGE IIB ACCORDING TO POSTOPERATIVE STAGING

Class	*No. of patients*	*Comments*
A	1	Living without apparent disease. Staging reduced from IIB (L of N) to A (postop.) by radium
Ao	1	Living without apparent disease. Staging reduced by radium
D	1	Died 34 days postoperatively of carcinoma and diabetes

TABLE XII.—FIVE YEAR SURVIVAL: RADIATION VERSUS SURGERY

	Stage I Per cent	*Stage II Per cent*	*Total Per cent*
Radiation			
Stockholm*	77	36	
M.G.H. and Pondville†	55	44.1	
Free Hospital for Women*	58	33	
Surgery			
M.G.H. and Pondville‡	81	58.7	73
Free Hospital for Women§	84.7**	80††	83.8

*1939-1948.
†1942-1949.
‡1940-1949.
§1943-1953.
**1 patient has pelvic recurrence.
††Not 5 year follow-up; 1 patient has vaginal recurrence.

Since these figures are better than any reported to date, the reluctance of Meigs to include radiation therapy may be questioned.

Incidentally, the number of fistulas in those patients who *had* radiation preoperatively (with or without cancer at the time of operation) was lower in Meigs' group (and in ours) than in those treated purely by surgery.

A comparison of survivals at the Free Hospital for Women and Massachusetts General and Pondville Hospitals is illustrated in Table XII. The Stockholm figures (all radiation, 1939 to 1948) are also indicated. It is evident that patients in stage I treated by radiation fared better at the Radiumhemmett than at the 3 Boston hospitals. In stage II the statistical difference was not marked. Comparison of radiated cases and surgically treated cases is always distorted by variables not readily visible. Thus the thinner, younger, good risk patients of stage I may have been treated by hysterectomy whereas the others, declined by the surgeon, were referred to the radiologist. In any event, Meigs' 5 year surgical "cures" were about the same as Stockholm's in stage I but considerably better than his own cases treated radiologically. It is difficult to state whether the surgical results in stage II demonstrate statistically valid improvement. The stage I cases treated surgically at the Free Hospital for Women show appreciable improvement over our own (but not Stockholm) patients treated radiologically. One patient in our stage I group is surviving 5 years but has a bladder recurrence so that our "cure" rate here is 81.1 per cent instead of 84.7 per cent. It is not appreciably different from Meigs' in a slightly smaller series (85 patients as against 104). Stage II (Free Hospital for Women) is shown as having an 80 per cent survival but these are not all 5 year follow-ups, and 1 of the living patients has had a vaginal recurrence recently treated. It will undoubtedly drop down to the 50 per cent survival since the total number treated is small and 1 death will markedly alter the results.

In summary, then, it may be stated that 105 patients were treated by radical hysterectomy and pelvic lymphadenectomy over an 11 year period. The operative mortality was minimal—1 patient. Morbidity and complications were of moderate severity, the major difficulty being the development of urinary fistulas in 7.6 per cent. This figure compares favorably with an incidence of 7 per cent quoted by Meigs and 23.5 per cent noted by Brunschwig. One should, however, remember the serious complications and sequelae of radium and x-ray such as proctitis, cystitis, fistulas, ileitis, bowel obstruction, and bowel necrosis. In this hospital severe reactions of this degree have been noted in 6 per cent of our patients treated radiologically.

The 5 year "cure" rate of 81.1 per cent in stage I cases is a definite improvement over previous 58 per cent in cases treated radiologically. Continued improvement is desired although recent changes in radium equipment and administration will undoubtedly increase the survival rate and diminish the complications. The answer still lies in proper selection of patients, some for radiation alone, others for surgery alone, and still others for combination therapy.

Our best results occurred when preliminary radium (3,000 to 3,500 milligram hours) was followed in 2 to 3 weeks by radical hysterectomy and the excised specimen contained no viable tumor and the nodes were negative. If the nodes are positive postoperative x-ray seems to be of value in increasing survival.

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A CLINICOPATHOLOGIC STUDY OF LARGE BENIGN GASTRIC ULCERS

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THE DICTUM that large ulcerating gastric lesions are almost certainly malignant was accepted in the medical literature for several decades. Only in recent years have scattered reports called attention to the entity of the large benign gastric ulcer. Because of the small number of histologically proved cases of this type reported, it was decided to undertake a clinicopathologic study of a relatively large group of these cases.

MATERIAL AND METHOD

The surgical files of the Mayo Clinic from 1940 through 1954 were examined for examples of chronic, benign gastric ulcer with a diameter of 4 centimeters or more and for which gastric resection had been performed. Measurements had been made by the surgical pathologist at the time of the original examination of fresh tissue. Cases of gastroduodenal and gastrojejunal ulceration were excluded. During this 15 year period there were 100 cases that met the aforementioned requirements. Data collected from the records and from gross and microscopic study of the surgical specimens form the basis of this report.

CLINICAL FEATURES

In the period covered by this study, 2,428 patients with benign gastric ulcer were treated surgically. Hence, the 100 cases of "giant ulcer" found represent 4.1 per cent of all cases of benign gastric ulcer treated surgically during this time.

The mean age of the patients was 53.2 years, the extremes being 3 months and 73 years. There were 78 males and 22 females, giving a ratio of approximately 3.5:1. Ninety-three patients presented a symptom complex that was suggestive of peptic ulcer, namely an intermittent, ulcer type of distress that occurred postprandially and that was relieved by ingestion of food or alkali. A relatively long duration of symptoms prior to surgical therapy was found in most cases. Forty-five patients had been symptomatic for 5 years or longer prior to operation. The mean duration of symptoms was approximately 6 years. Thirteen patients had been operated on previously. One of these 13 patients had undergone exploration and had been declared to have an inoperable gastric carcinoma although histologic proof was lacking. The same patient returned 6 years later because of persistence of epigastric pain, and subtotal gastric resection was successfully carried out for a large ulcer which histologically proved to be benign. The mean loss of weight for the 56 patients on whom this information was recorded was 24.5 pounds. Gastric hemorrhage as manifested by hematemesis occurred in 26 patients. Vomiting was a significant symptom in 51 patients. Seventeen patients had a palpable epigastric mass on physical examination. The remainder of the physical findings were not significant.

The most frequent clinical diagnosis was that of carcinoma of the stomach (carcinoma or questionable carcinoma), which was made in 45 cases. On the basis of roentgenologic

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TABLE I.—LARGE BENIGN GASTRIC ULCER: DISTRIBUTION OF CASES ACCORDING TO LOCATION AND SIZE OF ULCER

Diameter, cm.	*Total cases*	*Lesser curvature*			*Middle posterior wall*	*Posterior wall, greater curvature*	*Anterior wall, posterior wall**
		Posterior wall	*Straddling*	*Anterior wall*			
4.0– 4.4	57	30	24	2		1	
4.5– 5.9	7	3	4				
5.0– 5.4	19	13	5		1		
5.5– 5.9	1	1					
6.0– 6.4	9	5	2	2			
6.5– 6.9	1		1				
7.0– 7.4	5		3			2	
10.0–10.4	1						1
Total	100	52	39	4	1	3	1

*One ulcer involved both the anterior and the posterior wall.

findings, carcinoma was suspected in 40 cases, and benign gastric ulcer was correctly diagnosed in 45 cases; various other benign conditions accounted for the remainder of the roentgenologic diagnoses. Gastroscopic examination was performed infrequently but it did not appear to be of value in the diagnosis of large ulcers. The mean free gastric acidity was less than normal in males by 5.1 units and in females by 10.2 units. Likewise, the mean total acidity was reduced by 5.7 units in males and by 13 units in females. Seven patients had apparent achlorhydria as determined by studies with the Ewald meal; the effect of histamine was not tested in this group. Hemoglobin value and erythrocyte count were normal in the majority.

The surgeon definitely stated prior to resection his opinion as to whether the lesion was benign or malignant in 24 cases. An erroneous diagnosis of carcinoma was made in 13 of these 24 cases (54 per cent). These ulcers were characterized by the presence of sizable masses of inflammatory tissue in which large ulcer craters were palpable and which felt very firm. The Billroth II type of gastric resection was the procedure most frequently employed (76 cases). Anterior and posterior anastomoses were done in almost the same number of cases. The base of the ulcer was frequently left in situ in the treatment of large perforating ulcer of the posterior wall after examination of fresh frozen sections had revealed the benign nature of the lesion.

The hospital mortality rate was 7 per cent (7 deaths). Necropsy studies disclosed the cause of death to be generalized peritonitis in 6 of the 7 cases. The remaining death was due to bronchopneumonia with an associated renal shutdown. Total gastrectomy was the operation performed on 3 of the 7 patients who died.

PATHOLOGIC FEATURES

In 95 cases the ulcers were located on or near the lesser curvature and in 57 cases they involved the posterior wall (Table I). Examination of the gross specimens showed that usually they were nearer the pylorus than the cardia. In 3 cases a benign ulcer 4 centimeters or more in diameter was located on the greater curvature. The average diameter of the entire series of ulcers was 4.7 centimeters, the largest being 10 centimeters. There appeared to be nothing particularly characteristic of the distribution of the cases according to size of the ulcers (Table I).

In 66 cases the ulcer had perforated or penetrated. The organ most frequently involved by perforation was the pancreas, the liver being next in frequency (Table II). In 42 of the 66 cases (64 per cent) the ulcer involved the posterior wall and in the remaining 24 cases it straddled the lesser curvature.

The majority of the ulcers had circular outlines with sharp edges. An occasional oblong form was noted. The floor of the crater was smooth but extremely indurated and thickened and its depth often equalled or exceeded the thickness of the inflamed gastric wall. The margins of the crater were smooth and overhanging. Occasion-

TABLE II.—LARGE BENIGN GASTRIC ULCER: ORGANS INVOLVED BY PERFORATION

Organ	*Cases, per cent*
Pancreas	45
Pancreas and liver	8
Pancreas and transverse mesocolon	3
Liver	3
Pancreas and spleen	2
Transverse mesocolon	2
Liver and transverse mesocolon	1
Liver, pancreas, and anterior abdominal wall	1
Reduplicated portion of stomach	1
Total	66

ally the overhanging mucosa touched the base of the crater. The surrounding gastric rugae appeared to run directly up to the actual margin of the ulcer and stop. In the serosa of the gastric wall overlying the ulcer there were thickened, scarred areas and an occasional whitish plaque. These changes involved areas often larger than the ulcer crater itself. Multiple gastric ulcers were present in 4 cases but no more than 2 chronic gastric ulcers were present in any 1 case. Associated duodenal ulcers were found in 19 cases at the time of surgical exploration.

Microscopic examination of the mucosa adjacent to the ulcer showed varying degrees of gastritis with associated hyperplasia of mucous glands, cystic glandular disorganization, and rather marked prominence of foci of lymphatic tissue in the base of the mucosa. The floor of the ulcer consisted of four rather indistinct zones: (1) a zone of purulent exudate, (2) a zone of fibrinoid necrosis, (3) a zone of granulation tissue, and (4) a zone of fibrous tissue. Signs of secondary cytoplasia, namely glands with atypical hyperplastic cells and large nuclei and nucleoli, were equivocal. This observation is believed to be due to the fact that the material which we studied was preserved in formalin. The arteries at the base of the ulcer frequently showed an obliterative type of endarteritis.

COMMENT

Since the work of Alvarez and MacCarty in 1928, gastric ulcers 4 centimeters or more in diameter have frequently been considered malignant. Among 638 benign gastric ulcers (all removed by resection), they found only 2 benign ulcers as large as 4 centimeters in diameter. Knowing the percentage distribution of benign and carcinomatous ulcers according to size, they calculated that a gastric ulcer 4 centimeters in diameter was almost 15 times as likely to be malignant as benign. Further, they stated that "it is doubtful whether benign ulcers (excluding the gastrojejunal, the recurrent, and the syphilitic) ever grow much larger than a silver dollar (3.7 cm. in diameter)." The opinion that large gastric ulcers are nearly all malignant is shared by others.

The cases found in the present series are representative of the changes that have occurred in the surgical therapy of gastric ulcer during the past 28 years. At the time Alvarez and MacCarty made their report, gastroenterostomy was done frequently for gastric ulcer, whereas at present gastric resection is employed almost routinely. Hence more large benign gastric ulcers are now available for pathologic study.

While the frequent association of large size and malignant change in gastric ulceration is well known to clinicians, in the individual patient large size alone does not necessarily signify that the lesion is malignant, as is evidenced by the cases in the present series. Nevertheless, that size is an important point clinically in deciding the management of a lesion cannot be denied.

The clinical findings in the present series of cases were characterized by a relatively long duration of symptoms (in 45 per cent of the cases they lasted longer than 5 years), a fairly high incidence of hematemesis (26 per cent of cases), and a large loss of weight (mean loss of 24.5 pounds). These findings are in accord with those of Marshak, Shoulders, and their associates.

Branwood has stated that patients with large benign gastric ulcer are prone to have other chronic diseases such as tuberculosis, syphilis, and hypertension. Krisnapoller has expressed the belief that the patient who has a large benign gastric ulcer is more likely to have skin and cardiovascular diseases than

the patient who has a small ulcer. These diseases were not found to be present to any significant extent in the present series, however.

The entity of the large benign gastric ulcer needs to be recognized by the clinician, the radiologist and the surgeon. This is evidenced by the fact that clinically almost half of the patients in the present series were suspected of having carcinoma, and radiologically slightly more than a fourth of the patients presented what was interpreted as evidence of carcinoma. Further, in more than half of the cases in which the surgeon recorded his impression after palpating the lesion, an erroneous diagnosis of carcinoma was made. This and the fact that in 1 case the lesion was diagnosed as an inoperable malignant growth at the time of exploration without the benefit of histologic diagnosis re-emphasizes the necessity of having microscopic confirmation of the diagnosis. The employment of fresh frozen sections is important in this connection, since a definitive diagnosis can almost always be made in a matter of minutes by this means.

The reduced values for gastric acidity found in the cases of this series are in agreement with the work of Vanzant and associates who found that in the presence of gastric ulcer the mean free acidity was reduced by an average of 5.4 units in the male and 6.6 units in the female.

Early surgical intervention is indicated in the treatment of large gastric ulcers because of the uncertainty of the clinical diagnosis, the danger of massive hematemesis, and the failure of defects of this size to heal on a medical regimen. Excision of the lesion by subtotal gastric resection when possible appears to be the procedure of choice. The personal preference of the individual surgeon for an anterior or posterior anastomosis appeared to determine which procedure was done with the Billroth II gastric resection.

It is well for the surgeon to be mindful of the fact that a large perforating lesion may occasionally be benign. Thus it seems reasonable to establish the diagnosis of malignancy by study of frozen sections before extensive and radical resection of the stomach and adjacent structures for an ulcerating type of gastric lesion is performed. If the ulcer is benign, the base of the crater may be left in place on the pancreas, liver, or other structures as the case may be, and an operation suitable for a benign lesion carried out. Such practice would avoid the occasional instance in which a more radical procedure with its attendant increase in morbidity and mortality is performed for what actually is benign disease.

The hospital mortality rate of 7 per cent points out the technical difficulties encountered in the excision of large gastric ulcers. This is in contrast to a corresponding rate of 1 per cent for gastric resection for benign gastric ulcers of all sizes during 1954 as reported by Priestley and associates. The fact that total gastrectomy was the operation performed in 3 of the 7 patients who died no doubt accounts in part for the mortality rate experienced in this group of patients.

The gross and microscopic pathologic findings in these cases were similar to those described in the literature for chronic gastric ulcer except for the presence of unusual amounts of fibrous tissue in the bases of the ulcers in this study.

Whereas large benign gastric ulcers may occur anywhere in the stomach, it would seem from the findings in this series and from the work of Pero and associates and Caruolo that a large gastric ulcer involving the lesser curvature and posterior wall without obvious signs of malignancy at the time of exploration should not immediately be placed in the malignant category because of its size alone.

SUMMARY AND CONCLUSIONS

This is a report of the results of a clinicopathologic study of 100 cases of benign gastric ulcer 4 centimeters or more in diameter encountered at the Mayo Clinic. These cases constituted approximately 4 per cent of the cases of benign gastric ulcer treated surgically during the 15 year period 1940 through 1954.

The most significant clinical observation was the ability of the large benign gastric ulcer to simulate carcinoma, which points up the need for the clinician, the radiologist, and the surgeon to become aware of and to recognize the entity of such ulcers.

Although there is a definite correlation between the size of an ulcer and the likelihood of its being malignant, size alone, no matter how suggestive, is not an absolute criterion of malignancy in the individual case, as evidenced by the cases in this report. However, since the incidence of benignancy among gastric lesions whose longest diameter measures 4.0 centimeters or more is so low, immediate surgical therapy is advisable.

Unfortunately, a large benign gastric ulcer cannot always be distinguished from a malignant one by clinical means and by palpation at the time of operation. Nevertheless, when the surgeon finds a large gastric ulcer on the lesser curvature or the posterior wall, or both, without obvious signs of malignancy, he should not consider the lesion to be malignant because of its size alone. Further, the lesion should be treated by subtotal gastric resection if possible.

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EDITORIALS

THE HERITAGE OF WALTER WHITEHEAD

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FAME COMES TO FEW SURGEONS and to fewer still the honor of having operations known by their names. Walter Whitehead,[1] Professor of Surgery at Victoria University, Manchester, England, from 1892 to 1900, twice attained this eponymous distinction. His operations upon the tongue and upon the anal canal for hemorrhoids were once widely used. In 1902, Doctor Alexander of New York moved a vote of thanks to Professor Whitehead for his presidential address at the meeting of the British Medical Association and said "there is not a textbook of surgery used in our medical schools which does not bear upon its pages the records of his contributions to operative surgery, and among the earliest names which the students of medicine in America learn is that of Walter Whitehead."

Time has not dealt kindly with his contributions. Other methods have supplanted his resection of the tongue, and his name is execrated among proctologists because the total excision of the pile-bearing area which he advocated, resulted so frequently in severe postoperative stricture. Reference to his surgical papers, however, mitigates these criticisms. Not all his hemorrhoid operations were radical. "Wherever it is possible with strict regard to removing every evidence of haemorrhoidal growth (*sic*) I invariably leave longitudinal strips of mucous membrane continuous with the skin."

[1]WHITEHEAD, W. The surgical treatment of haemorrhoids. Brit. M. J., 1882, 1: 148–150.

Whether in the conservative or radical operation, however, he introduced three important principles: Firstly, skin removal was very conservative and this is the antithesis of the ligature operation in which skin removal is considerable. Secondly, hemostasis was achieved, not by mass ligation of the pile at its pedicle with heavy silk, but by clamping the individual vessels and twisting them. Thirdly, primary closure of the wound was effected without tension by "several fine silk sutures." Whitehead was insistent that neither secondary hemorrhage nor stricture formation occurred. It is difficult to see how sepsis was avoided with these concomitants.

Be that as it may, during the last 10 years an attempt has been made to apply the Whitehead principles to the hemorrhoid operation by using colon lavage and an antibiotic regimen, both oral and parenteral, such as is employed prior to colon surgery. The incisions are so placed that most of the skin on the pile is retained and the subsequent suture line lies without tension at the level of the "white line." The vessels are isolated and ligated with fine catgut. A continuous fine catgut suture is employed to close the wound where the primary pile (and its attendant secondary piles) has been removed. There are thus 3 anal suture lines as a rule, shaped like a triangle.

The following facts were noted: Sepsis was absent. The meticulous preservation of skin resulted in a high suture line (at the "white line") and a normal anal appearance. Post-

operative pain was readily controlled by the frequent application of topical (locally acting) anesthetics instead of hypodermic injections. Urinary retention was very rare and secondary hemorrhage was unknown. An early movement of the bowels on the second day was sought as no tubes, gauze, or other impedimenta were required in the anorectal canal. The patients could be discharged between the fourth and seventh days, being instructed to maintain a high standard of hygiene and to apply the topical anesthetic ointment frequently. No postoperative digital dilatation was required as healing occurred by first intention and stricture was not encountered. Oral antibiosis was continued until healing was complete.

As Whitehead pointed out, if skin is removed in this procedure to the extent which customarily attends the ligature operation, stricture will frequently occur on account of the disruption of the tense suture line and the subsequent healing per secundam. The operation has been successfully carried out for leucoplakia and papillomatosis of the anal canal, a point which serves to emphasize the fact that mucosal removal can be extensive without danger of stricture. "I have no fear" says Whitehead, "of the bowel being inconveniently contracted when mucous membrane alone is sacrificed, and I believe that undue contractions only take place when annular cicatrix is formed at the expense of integument."

The success which attended this approach encouraged the application of Whitehead's principles to chronic fissure in ano. The fissure was excised, the sphincter reconstructed, if necessary, and the bare area covered by transposing a thin pedicled skin and fat flap from the adjacent perianal tissues. The donor area was closed by apposition, and the transposed flap was fixed in position by 2 fine silk and several fine catgut sutures. The 2 silk sutures are of importance. One fixes the tip of the flap to the apex of the anal wound, the other is a longitudinal mattress suture holding the base of the flap against the underlying fascia to obviate dead space and tension. The antibiotic regimen is imperative, and oral antibiosis is continued until the silk sutures are removed on the tenth day. This is a most satisfactory operation.

Every surgeon will agree that fistula in ano is in a different category. There are a number of cases, particularly of blind external fistula and fistulas with a single, short track and low internal opening, which are adapted to primary closure (with temporary wound drainage). Conversely, primary closure is destined to failure under other conditions. These include cellulitis, tuberculosis, and incomplete removal of the tracks (especially the submucous and supramuscular components). However, recurrent fistula in ano in a scarred ischiorectal fossa does not present much prospect of permanent cure with prevailing methods of incision and packing. In these circumstances, the removal of all scar with its replacement by fresh tissue is an important factor in preventing recurrence, in permitting restoration of the anal musculature damaged at previous operations and in eliminating epithelial crevices consequent upon prolonged packing. Three sources of replacement tissue have been satisfactorily used. For small unilateral defects in the ischiorectal fat either the gluteal fat or a portion of the gluteus maximus muscle may be turned into the defect as a pedicled flap. For large and bilateral defects the gracilis muscle is ideal. The latter is divided through its tendon of insertion and turned back upon itself in a subcutaneous tunnel leaving its proximal attachment (with its blood supply and innervation) intact. All such wounds are drained with 1 or more fine drains for a few days to avoid hematoma formation which encourages recurrence. The superficial wound is closed with interrupted silk sutures both on the perineum and in the anal canal.

It may not be idle to reflect that in our own surgical generation the removal of the diseased lung has progressed from mass pedicle ligation to dissection, ligation, and bronchial closure in seeking healing per primam. The humble pile may follow suit.

JUVENILE MELANOMAS AND MALIGNANT MELANOMAS

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THE NATURAL CONSEQUENCE of many contributions involving major changes in concepts of therapy or of diagnoses is a tendency, for a while at least, toward a less discriminate application of criteria than is warranted by the character of the contributions. The problems of nevi and malignant melanomas represent a case in point. In the last few years there appears to have been achieved a considerable degree of clarification of the histologic criteria for the diagnosis of the various pigmented nevi and malignant melanomas. However, the effective use of such criteria in all laboratories is not an automatic process. Quite apart from the controverted issue of histogenesis, the current principal sources of errors, questions, and disagreements involve the following: (1) The histologic criteria for the diagnosis of (a) juvenile melanomas of children and adults, (b) melanocarcinomas of children, and (c) the primary versus the metastatic melanocarcinoma; (2) the definition and prognosis of the superficial melanocarcinoma; (3) the *de novo* origin of melanocarcinomas; (4) the relationship of the experimental "melanoma" to the human lesions; (5) the influence of hormonal changes on nevi and melanocarcinomas; (6) the questionable evidence from the use of tyrosinase in the differentiation of junctional nevi from malignant melanomas; and (7) therapy.

All of the foregoing has been discussed to some degree in our previous publications.[1] However, because of the great practical importance of the widely prevalent misconception that it is impossible to differentiate the benign juvenile melanoma from the melanocarcinoma, this phase of the problem is selected for added emphasis and evaluation.

For many years it has been taught that moles of children may look malignant histologically yet, paradoxically, behave as benign lesions. In other words, because it has been assumed as fact that malignant melanomas either did not occur or, at most, occurred with extreme rarity in children, the histologic diagnosis of prepubertal melanocarcinoma was accordingly considered by the surgeon to represent an innocuous lesion, and both surgeon and pathologist were resigned to this clinicopathologic paradox which was regarded simply as just one more limitation of the microscope. The situation up to this point was summarized in 1948 in an editorial by Pack.[2] It happens that in this same year, the histologic characteristics of these benign juvenile melanomas were defined for the first time by the late Sophie Spitz.[3] Briefly, these criteria included chiefly edema, lymphangiectasia and telangiectasia, and hyalinization of the upper cutis; certain forms of giant cells; relatively bland and interrupted junctional change; pseudoepitheliomatous hyperplasia; large, discrete, epithelium-like clusters of round, polygonal, or spindled cells within the upper dermis commonly associated with collections of lymphocytes and histocytes; and, finally, a paucity of melanin pigment in the vast majority of the lesions. The applicability of Doctor Spitz's contribution was enormously increased when it was subsequently discovered that occasionally the juvenile melanoma persisted into adult life, or possibly developed after puberty in some patients.[1] In the past, the fact that the patient happened to be an adult was thought to eliminate the possibility of juvenile melanoma and arbitrarily led to the diagnosis of malignant melanoma. The

[1] ALLEN, A. C., and SPITZ, SOPHIE. Malignant melanoma, a clinicopathological analysis of the criteria for diagnosis and prognosis. Cancer, 1953, 6: 1–45.

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[3] SPITZ, SOPHIE. Melanomas of childhood. Am. J. Path., 1948, 24: 591–609.

direct and obvious consequence of such mistaken diagnoses included unnecessarily radical treatment and unwarrantedly grave prognoses. To date, we have seen 34 examples of these benign, juvenile melanomas in adults. Unfortunately, no data regarding the endocrinologic status of these patients are available. There were approximately equal numbers of men and women in this group. The histologic picture of the juvenile melanomas of adults is indistinguishable from that of children except for the tendency of some of the lesions of adults to show evidence of involution in the form of interspersed fibrosis. The juvenile melanomas having now been shown to occur in adults would seem to answer negatively the question as to whether or not cells of the juvenile melanomas of children, which histologically simulate malignant cells, would acquire biologically malignant behavior if they were transplanted to an adult hormonal environment. Finally, it should be mentioned that contrary to the conclusion of others, the evidence indicates that there is no more likelihood for a juvenile melanoma to undergo cancerous change in adult life than for any other compound nevus.[1] Nevertheless, in order to focus attention on the histologic resemblance between the juvenile melanoma and the malignant melanoma, the designation "melanoma" was retained and when qualified by "juvenile," indicates, as stated, a clinically benign lesion.

The second significant ramification of the histologic definition of juvenile melanoma concerns the diagnosis of melanocarcinomas of children. The fact is that we have personally seen 9 such clinically proved malignant melanomas, and almost an equal number has been observed by others. In view of the fact that aggressive melanocarcinomas of children do occur—and apparently, although uncommon, their incidence is greater than formerly believed—what, then, is a surgeon to do when his pathologist diagnoses a lesion of a child as follows: "Malignant melanoma histologically, but I predict a benign clinical course in view of the fact that the patient is prepubertal"? Such diagnoses are as common as they must be bewildering to all concerned. Actually, the potentialities inherent in the histologic criteria of juvenile melanomas and melanocarcinomas of childhood permit their differentiation with reasonable confidence after adequate experience with such lesions. Their distinguishability was vividly demonstrated several years ago by Doctor Spitz, who, from a large group of unknown slides submitted from another medical center, correctly segregated the melanocarcinomas of children from the juvenile melanomas. In briefest terms, the diagnosis of the melanocarcinoma is based predominantly on the absence of the aforementioned landmarks of the juvenile melanomas and on the presence of an aggressive histologic appearance of both the intradermal and epidermal components. Perhaps one of the most revealing clues to the diagnosis of the malignant melanoma of childhood is the evidence of accentuated activity in the area of the epidermal junctional change as well as the presence of isolated anaplastic cells in the uppermost epidermal layers.

From the point of view of pathogenesis of these unique lesions of children, interest naturally has long been directed toward the influence of hormones. Of particular pertinence in this connection is the 5 year old negro boy, recently observed in our institution, who had a melanocarcinoma of the buccal mucosa in association with an androgenic adrenal cortical carcinoma. In the light of this association, and in view of the reported activation of nevi during pregnancy and in the presence of melanocarcinoma, as well as the appearance of junctional nevi following the administration of ACTH and cortisone, a thorough study of the endocrinologic status of children with melanocarcinomas, and perhaps also of adults with juvenile melanomas, would appear indicated.

[1]Loc. cit.

THE SURGEON AT WORK

ABDOMINAL DRAINAGE AND THE AIR-VENT SUCTION TUBE

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"DRAINAGE OF THE PERITONEUM, one of the most important subjects in abdominal surgery, is yet one which stands in a most uncertain position." So wrote Charles Bingham Penrose in 1890. He added that "it is desirable to use a tube combined with a capillary drain of gauze or wick," and the now famous Penrose drain was thus introduced.

Abdominal drainage is still a controversial problem. No clear-cut indication yet exists and, as Penrose pointed out, "the necessity for drainage depends to a great extent upon the operating surgeon." Lazarus in 1954 attempted to determine the present concept of intraperitoneal drainage by sending a questionnaire to 100 leading surgeons in this country. Noting a fair measure of difference of opinion, he concluded, just as Penrose did 65 years before, that the decision as to drainage is made on a purely personal basis.

Not only have opinions on when to drain differed widely, as expressed by axiom, "When in doubt, drain," or as modified by Mayo, "When in doubt, don't drain"; but, opinions on what type of drain to use also have differed sharply.

REVIEW OF LITERATURE

Hippocrates first described drainage tubes or cannules for use in the treatment of empyema. Celsus treated abdominal ascites by tubes of brass or lead. They were conical to prevent slipping into the abdomen and were filled with plugs to regulate the outflow. Paré, in the sixteenth century, devised tubes of gold or silver with a collar flange. In 1719, Heister first used wicks in conjunction with tubes and thus introduced capillary drainage.

As operators began opening the abdomen more frequently in the early nineteenth century, following McDowell's ovariotomy, they sought methods to reduce the rather high mortality. Keith well expressed the problem of the time: "The red serum, the enemy of the ovariotomist." Peritoneal drainage was a major problem, and Sims in 1866 began drainage through the vagina. At this time, Chassaignac introduced an important innovation by using soft rubber tubes in surgery.

In 1906, Yates reviewed the entire problem of peritoneal drainage and, following careful experiment on animals, decided that drainage of the general peritoneal cavity is physically and physiologically impossible. Peritoneal drainage, he concluded, must be local.

Coffey, in 1907, studying the problem of posture in abdominal drainage, followed the recommendations of Fowler, who advocated elevating the bed to from 8 to 14 inches to drain fluid into the pelvis. Using the cadaver and casts, Coffey showed, by very careful work, that the lowest point in the peritoneal cavity with the patient flat was not the pelvis but the flank, which is 1 inch deeper. Thus, to drain the fluid from the flank to the pelvis, the upper end of the body must be elevated to an angle of from 60 to 70 degrees. Furthermore, he demonstrated that either the flank or gutter holds more fluid than the pelvis when the subject is lying on his back. He evolved the "rubber dam" to draw the fluid to a low point in the reservoir.

Williamson found that by emptying the abdomen by gravity, that is, with the patient lying on his face, the mortality in cases of ruptured ap-

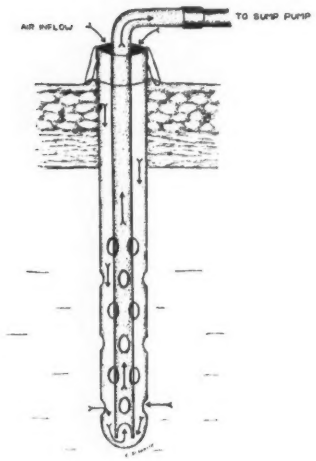

FIG. 1.

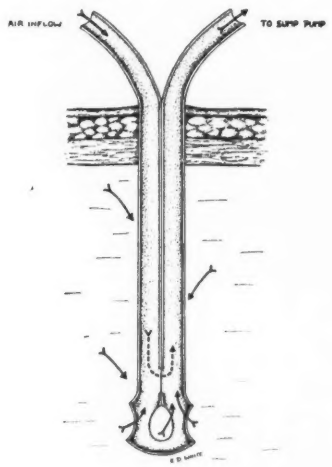

FIG. 2.

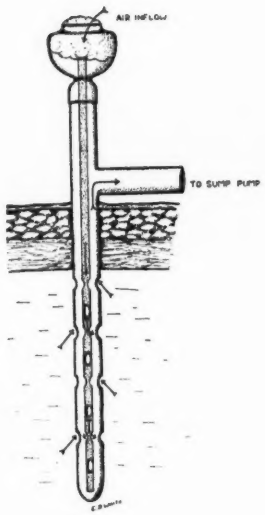

FIG. 3.

FIG. 1. The sump drain introduced by Babcock who used stainless steel and air-vent suction for abdominal drainage.

FIG. 2. The double-barrel drainage tube of Chaffin. Tube is placed in the low part of the abdomen and fluid aspirated, aided by air passing through the open limb.

FIG. 3. Double-lumen tube placed in abdominal cavity for drainage. It is pliable and can be accurately positioned prior to closure.

pendix is reduced from at least 20 to about 4 per cent.

AIR-VENT SUCTION

One of the first advocates of air-vent suction was Wayne Babcock. In 1938, he reported the use of a large glass cylinder, the so-called lamp-chimney drain (used by Deaver in 1905), to collect pus and fluid from the peritoneal cavity. He found that air passing through such open glass tubes did not have a grossly harmful effect upon peritoneal surfaces.

Later, Babcock introduced stainless steel fenestrated tubes with suction applied (Fig. 1). Thus evolved the sump (or marsh) drain. Further work by Burnett demonstrated that such drainage in the presence of peritoneal infection was an important method of reducing morbidity and mortality.

At this time Babcock pointed out that peritoneal fluid remote from a localized abscess is often sterile and might best be left undisturbed. Thus, by draining the pelvis or other parts of the peritoneal cavity infection was frequently introduced.

Chaffin, in 1940, emphasizing the use of suction in drainage of cavities, pointed out that no cavity can be emptied completely and continually unless air is admitted. His contribution was the double-barrel drainage tube, in which air was introduced into one limb and suction was applied to the other limb as illustrated in Figure 2.

Following total gastrectomy, Wangensteen advocated the use of air-vent suction in the splenic bed. He believed that such air-vent suction near the anastomosis shortened the hospital stay by 7 to 10 days because it prevented inevitable collections.

RUBBER AIR-VENT TUBE

My interest in air-vent suction drainage was prompted by several sets of events in which conventional types of drains failed to evacuate or to signify the collection of fluid or blood. In one particular instance, the abdominal wall was closed too tightly around the drain, and in still another instance, the omentum had prevented the free accessibility of pus to the outside.

The rigid stainless steel air-vent tubes frequently seemed cumbersome, and positioning them in a gutter or cavity was difficult. Therefore, I employed a rubber tube (Fig. 4) which was designed for air-vent suction and which combined the features of Chaffin's methods with the features of Babcock's rigid stainless steel sump drain.

One of the principal features is the small inner tube acting as the air vent, the top of which is a bulb and is made to contain sterile cotton to filter out any gross particles which are found in the air.

After experimenting, I found it most desirable to place the air vent within the tube, much like Devine's intestinal air-vent tube.

The principle of the tube is the simple fact that for fluid to escape from a closed cavity, air must first enter unless the fluid is under pressure. The tube can best be demonstrated in a patient with ascites. When the abdomen is filled with ascitic fluid, or pus or blood, the fluid readily escapes through a single lumen if under pressure. However, once the pressure within the cavity reaches that of the atmosphere, the fluid will drain only by gravity or by suction. If one is to employ suction, air must first enter.

The tube is exteriorized through a stab wound and anchored to the skin (Fig. 3). A sump pump is attached for continuous suction. Exudate usually blocks the tubes within 48 to 72 hours, but if one suspects a collection has developed, the outer or inner tube is irrigated with an antibiotic solution and the tube reopened.

CASE REPORTS

The values of tubes is proved to my satisfaction in three types of patients: (1) those with ascites, (2) those who have undergone gastrectomy, and (3) those requiring drainage of an abscess. The feasibility of the tube can be demonstrated in patients with ascites. After the patient has had the routine aspiration, the air-vent suction tube is placed in the abdomen and suction applied. In the next 72 hour period, copious amounts of fluid are obtained, even though previous aspiration by conventional means was employed. In 1 patient, 5,000 cubic centimeters of ascitic fluid was obtained by routine tap. The air-vent tube was placed in the abdomen through a small opening, and 4,200 cubic centimeters were obtained during the next 72 hour period with changes in position and constant suction.

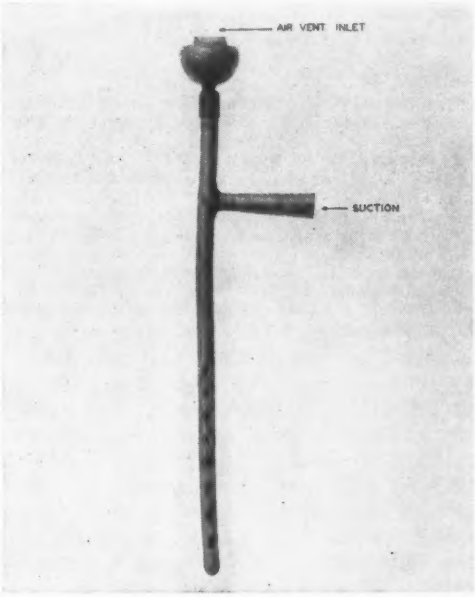

FIG. 4. Rubber tube designed for air-vent suction and drainage of abdominal cavity.

Patients with ruptured ulcers notoriously have considerable fluid in the peritoneal cavity and are excellent candidates for air-vent suction. The tube has been employed in such instances and 200 to 500 cubic centimeters of aspirate collected in the early postoperative period.

I agree with Wangensteen that air-vent suction is excellent for keeping the splenic bed dry following splenectomy and for avoiding possible injury to the tail of the pancreas. On one occasion when I used my tube after splenectomy which was done on a patient with a ruptured spleen, 525 cubic centimeters of fluid were collected in a 48 hour period.

The tube can be used in abscess following ruptured appendixes or pelvic abscesses with satisfactory results. Thick exudates or blood will clog the tube in 24 to 48 hours, and irrigation may be necessary.

After radical mastectomy, the tube may be placed under the skin for 24 to 48 hours and a rather surprising amount of blood or serum will collect.

SUMMARY

A brief review of drainage of the abdominal cavity is presented. Attention is directed to air-

vent suction of the peritoneal cavity. A double lumen rubber tube is described.

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CORRECTION OF THE "WHISTLE DEFORMITY"

GEORGE F. CRIKELAIR, M.D., and MAURICE J. HICKEY, D.M.D., M.D.,
New York, New York

STANDARD METHODS, such as described by Le Mesurier (3, 4) and Brown and McDowell, are well known and widely used in the primary repair of cleft lips. There are, however, few standard procedures for secondary revision of a cleft lip. Because the deformities are quite variable, so must the surgery vary to meet each individual problem.

Among the possible deformities which need revision after primary lip repair is the "whistle deformity." Here there is a fairly constant pattern for which a standard procedure can be used to advantage. This deformity not infrequently follows the repair of a complete or incomplete bilateral prealveolar cleft in which the lateral segments of the lip are sutured to the prolabium, retaining the vermilion of the prolabium as the center segment of the lip. There can be no criticism of this method of primary repair; rather, we believe it is the best technique for repairing the bilateral prealveolar cleft. The prolabium, even though very small at the time of initial repair, grows well and is likely to produce a lip which has a cosmetically pleasing length. It does not result in a long upper lip as occasionally occurs after lateral flaps have been added below the prolabium (Fig. 1). Likewise there follows no "trapdoor" elevation of the prolabium (Fig. 2). Schultz in 1946 described this repair for bilateral cleft lip with a modification to prevent the so-called "whistle deformity" by using lateral flaps for the under surface of the prolabium.

In the "whistle deformity" (Figs. 3 and 4a and b) the mucocutaneous line of the upper lip is even. The lateral portions of the vermilion beneath the mucocutaneous line are full and equal and are a good match with the full lower lip. The central or prolabial segment is lacking in vermilion fullness. As a result, with the mouth in a relaxed position, either a dark hole is seen or portions of the upper central incisors are visible, depending on the lighting.

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In attempting repair of this defect several possibilities can be visualized: (1) Removal of fullness of the lateral segments of the upper lip to match the central segment. This step would make the entire upper lip too thin as compared with the full lower lip. (2) Advancement of tissue from the full lateral segments into the centrally deficient area. This may be objected to for the same reason given in the first statement. (3) Addition of tissue from the lower lip. This step may detract from the fullness of the lower lip with possible imbalance as mentioned in statements 1 and 2. It would further require either a modified Abbe technique or a composite graft from the lower lip. The former adds a second operation, and the latter carries the added hazard of nontake or partial take of a free graft.

A more satisfactory procedure would seem to be a V-Y type of advancement which can be done in one operation. The mucous membrane along with the submucosa is advanced downward and outward as a flap based at the mucocutaneous line.

TECHNIQUE

Figure 5a is a sketch of the lip showing the "whistle deformity." Incisions are started almost

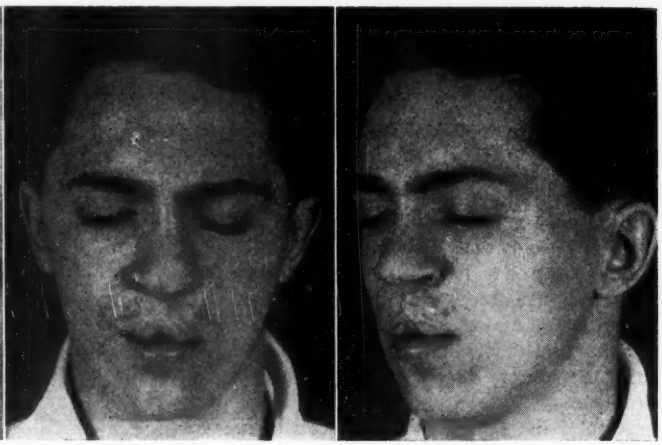
FIG. 1.

FIG. 2.

FIG. 1. Long upper lip following primary repair of a bilateral prealveolar cleft with lateral flaps rotated beneath the prolabium.

FIG. 2. "Trap door" elevation of the prolabial segment.

FIG. 3.



a b

FIG. 4.

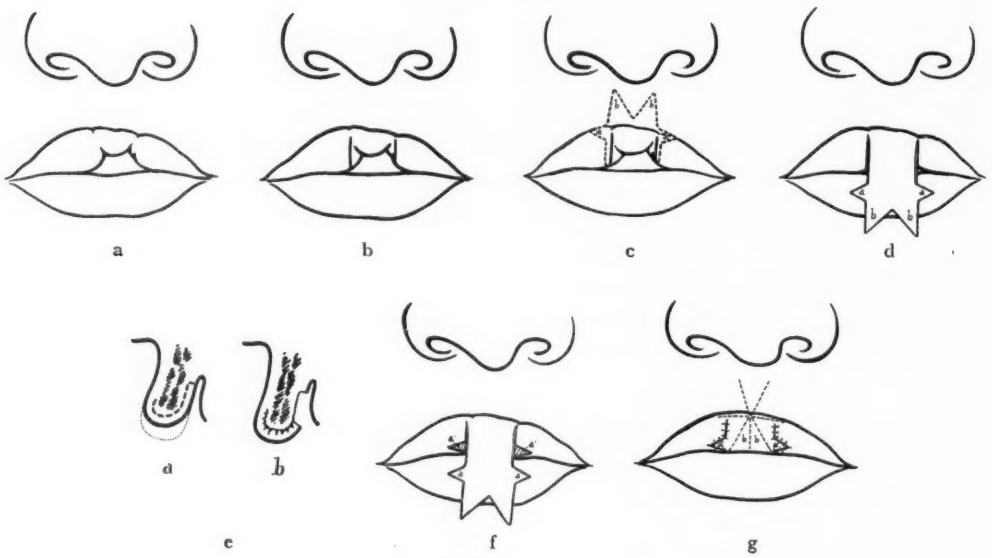
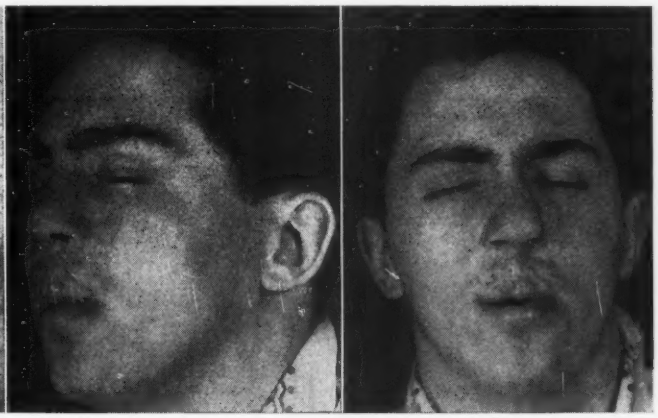


FIG. 5.

at the mucocutaneous line on either side at the junction of the central deficient segment with the full lateral components of the lip (Fig. 5b). These incisions are carried backward and upward in the mucous membrane around the free edge of the lip (Fig. 5c). A triangle flap is included bilaterally as marked (*a* and *a*) and each incision is carried almost to the apex of the buccal-labial sulcus. Here 2 larger triangles (*b* and *b*) are formed. Following these incisions, a fairly thick flap is raised (Fig. 5d). The flap is then advanced and put into position so that the central segment is equal in fullness to the lateral portions of the lip (Fig. 5e). The 2 small triangular flaps (*a* and *a*) are thus advanced downward and forward, that is, toward the mucocutaneous line.

FIG. 6.



a b

FIG. 7.

FIG. 3. "Whistle deformity" following V excision and closure of a bilateral incomplete cleft lip.

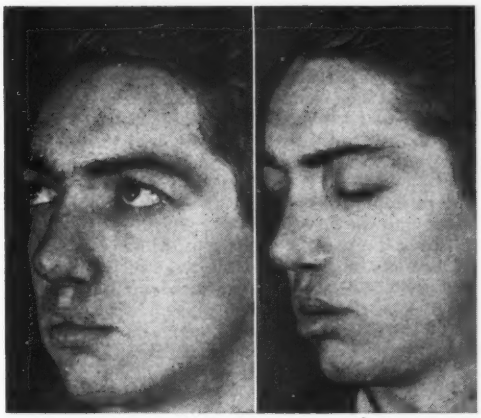
FIG. 4. a and b, "Whistle deformity" following repair of bilateral cleft lip.

FIG. 5. a to g, Drawings illustrating technique.

FIG. 6. Postoperative view of deformity shown in Figure 3 after revision of the central deformity by mucous membrane flap advancement.

FIG. 7. a and b, Postoperative views of patient shown in Figure 4a and b after repair of the central deformity by flap advancement. A revision of the nasal tip has also been done.

FIG. 8. a and b, Preoperative and postoperative views of "whistle deformity" after repair of a unilateral cleft lip.



a b

FIG. 8.

After the small triangles (*a* and *a*) are advanced forward, triangular wedges of mucous membrane of similar size are removed from the lateral segments of the lip (*a'* and *a'*) (Fig. 5f). The entire flap is then sutured into its new position with interrupted catgut sutures (Fig. 5g). The small lateral triangles (*a* and *a*) fit into the lateral segments of the lip. The larger triangles (*b* and *b*) are advanced and sutured together. With slight undermining, the under surface of the upper lip is sutured together in a stellate manner.

The operation can be done under nerve block anesthesia. No dressing is needed. There is apt to be considerable swelling of the upper lip postoperatively.

This procedure has been of value not only in secondary revisions of bilateral cleft lips (Figs. 6 and 7a and b) but also in an occasional unilateral lip repair (Fig. 8a and b) and in electrical deformities resulting from burns of the lip in which there has been a similar vermilion deficiency.

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Reviews of New Books

THE TEXT, *Ulcers of the Leg*,[1] is a laboriously written book covering the routine etiopathogenetic and therapeutic aspects of the common and the uncommon lower leg ulcers. Rather than simplifying, the author has chosen to try to make everything as complicated and detailed as possible. From a pedagogic standpoint, this detracts considerably from the practical value of the work and conceivably could lead to its use as a reference rather than a practical aid. The author is styled "Chief Professor Surgeon in the Faculty of Medicine of Barcelona," and as such, apparently believes that his personal opinions, interpretations, and theories make good textbook material. This reviewer decries the pontifical attitude displayed, especially when the statements made are generally well known, too often repeated, or possibly not in agreement with the facts.

In the organization of the material, the general features of the three etiologic types of leg ulcer are first described—the venous, arterial, and neurotrophic. A good deal of time is appropriately expended on the discussion of venous ulcers resulting from valvular incompetency. The author believes that all varicosities, whether essential or postphlebitic, are the result of one primary pathogenetic mechanism; i.e., are due to the existence of arteriovenous communications. He fails to recognize that others have proposed this before, and that it already has been rejected as an over-all concept by many critical observers in vascular surgery. Venous thrombosis and its sequelae are routinely covered with the addition of many personal views. The importance of deep insufficiency in the production of venous ulcers is described at length, but the author fails to recognize the true arrangement of the lower leg communicating veins. The work of Linton, Sherman, and of Cockett and Dodd has been entirely overlooked in this regard. Much attention is given to the influence of postural changes. The author believes that the normal individual, when erect, is on the verge of dependent peripheral edema. With respect to diagnosis of deep valvular incompetence, operative intravenous pressure studies and retrograde phlebography are used. In the local treatment, after conservative measures have failed, the author prefers the logical technique of excision and split-thickness skin grafting for such ulcers. Superficial varicosities are corrected by means of standard ligation and stripping of either or both saphenous systems as indicated. Deep incompetence is treated by "spaced ligations made under manometric control," a combination of superficial femoral and popliteal vein ligation. Although the author claims good results from this procedure, it should be pointed out that many others believe that deep venous ligation, in itself, has little effect on the course of ulceration and induration of the lower leg (Linton, 1953, Moore, 1953, Goligher, 1953, Cockett, 1953 and 1955, and Boyd and associates, 1954).

The second type, the arterial ulcer, is covered in the next 150 pages. These lesions include the traumatic, arteriosclerotic, "infective and lymphangitic" ulcers, the ulcers of thromboangeitis obliterans, Raynaud's disease, arteriovenous aneurysms, "chronic cutaneous ischemia," and others found in such unrelated conditions as Malta fever, chronic pernio, livedo reticularis, and poliomyelitis. When the ischemic factor is significant, he adds sympathectomy to the therapeutic program, but the local care is as previously outlined for venous ulcers. He concludes with a short section on the neurotrophic or plantar ulcers, and concludes that the therapeutic results are unsatisfactory.

This text represents a great deal of work and undoubtedly is a compilation or summary of experience previously recorded in various contributions to medical journals. Bibliographic material often is repeated and is found at the end of sections within chapters. Unfortunately there is considerable repetition, with instances of Spanish usage carried over into the English text, making reading sometimes difficult even for one who is well acquainted with this particular type of work.

One wonders why Vidal-Barraquer was not listed as coauthor of this text. He is constantly referred to as "my co-worker" throughout the text. He and the author wrote many articles together, and their names are noted in parallel on the jacket.

Perhaps further insight into the author's philosophy can be gained from the following paragraph (p. 317): "Patients with venous ulcers should not be operated until the complete healing of the ulcer is achieved by either a medical or surgical treatment. Nevertheless, to save time, we may operate on the venous system even without a complete healing of the ulcer."

Aside from the shortcomings mentioned, the illustrations and photographs are of good quality. The

[1] ULCERS OF THE LEG. By P. Piulachs. 574 pages, 303 illustrations. $15.50. Springfield, Ill.: Charles C Thomas, 1956.

book is well bound and printed on excellent paper. While it contains much excellent material, it suffers because of the style and manner of presentation. Although the next edition may well benefit from some condensation and a few additions, the present text is an excellent report on the care of leg ulcers under the direction of Piulachs in Barcelona.

Walter W. Carroll.

THE VERY COMPREHENSIVE VOLUME titled *Conjugal Sterility*[2] has many big name collaborators and as a result a most worthwhile contribution to South American literature is forthcoming. The subject matter of conjugal sterility is extremely important from a medical as well as social viewpoint. It is heartening to read that the approach to the question is not that of treating sterile women but directing the problem to the treatment of sterile couples.

The many factors causing sterility, some immediate and personal; others remote, environmental, and accidental are discussed quite thoroughly. The physiopathology of the sterile female is discussed after a consideration of the physiologic basis of fertilization. It is contended that it is extremely uncommon for sterility to be attributed solely to one cause, rather the rule being that two or three factors are responsible.

The statistical evidence upon which the many conclusions are drawn is based on the study of 700 couples registered at the Sterility Department of The Ramos Mejia Hospital, Buenos Aires.

Masculine responsibility for sterility of the conjugal couples was observed in 15.23 per cent, gonadic or canalicular factors averaging 6.02 per cent. Great importance is given anamnesis as a basic guide, the patient's personal and hereditary histories must be investigated thoroughly. Vaginal smear is emphasized, the patient being trained in obtaining her own specimens directly by manipulation of a bulbed cannula. Alterations in the pelvic cavity pre-eminently interferes with the fertilization mechanism, patency of the ovarian tubal hiatus being of the greatest interest. The methods of approach are dealt with in detail.

In considering treatment, each problem is viewed and handled specifically, with a consideration of general medical conditions and various surgical procedures. Definitely a valued contribution on the subject of conjugal sterility, this book is recommended regardless of the language barrier.

—Stephen W. Zieman.

THE THIRD EDITION of Lowsley and Kirwin's two volume *Clinical Urology*[3] appears in entirely new dress. The greater size of the pages in these volumes (although making a little more of a problem for the average bookcase) allows the books to be thinner and more easily handled. The arrangement of text, three columns to the page, enables easier and more rapid reading, as well as giving a more attractive appearance. In the effort to keep abreast of current material, books which pass through successive editions often become more or less patched up and a complete rewrite job is indicated. Despite minor indications that certain sections of this edition should be thoroughly rewritten, in general, the text has good continuity and an even tempo.

The outstanding contribution of the book is, of course, the illustrations of pathologic specimens and surgical procedures by the peerless medical illustrator, William P. Didusch. The authors state in the preface that these make the work a "veritable atlas of urologic pathology and surgical technic." Such is exactly what this book is, and it will remain incomparable in this regard. These superb illustrations of surgical procedures, and the descriptions likewise, will be most helpful to the student and practicing urologist alike. Probably no better collection of urologic surgical illustrations graces any book yet published. Some of the permanent value may be jeopardized, however, because of the use of ribbon catgut in so large a number of illustrations. This suture material has not had wide acceptance, and if it falls more or less into disuse, these illustrations will seem dated.

Diagnosis, it must be said—and especially urographic diagnosis—has been given far too little emphasis. For instance, the 30 pages of the chapter entitled "Roentgenography of the Genito-Urinary Tract" give woefully inadequate coverage for a book of this kind. Most of the few illustrations included in this chapter are produced as positives rather than negatives, which makes interpretation difficult. Most modern books reproduce roentgenograms as negatives so that they appear exactly as on the original film which the physician is accustomed to reading. Although it is suggested in this chapter that more and better urograms will be included in subsequent discussions of injury and diseases of the various urologic organs, few appear there. For instance, only 1 normal urogram is shown; yet the innumerable variations of the normal constitute one of the most confusing problems confronting the young urologist or student. Renal tuberculosis is illustrated by a group of only 4 roentgenograms, which are difficult to interpret because of being reproduced as positives, and which illustrate only advanced, "4+" pathologic changes of the old county-hospital variety. No illustrations of early minimal lesions so important in present-day diagnosis are included. Examples of such lapses could be multiplied indefinitely.

The organization is good. From Chapter 7 on, 3 chapters are devoted to each organ, proceeding inward from without (beginning with the penis). The 3 chapters devoted to each organ include: (1) embryology, anatomy, anomalies, and physiology; (2) injuries and diseases, and (3) operative and nonoperative treatment. Although this plan causes some overlapping (as, for instance, in the case of diseases which affect multiple organs), still any plan would involve the same difficulty.

Special mention should be made of the excellent summary of the physiology of the kidney (page 750, volume II). It is concise and well written, and from a few moments' reading the busy urologist may really

[2]ESTERILIDAD CONYUGAL. By Normando Arenas, Alberto E. Bettinotti, and Edmundo G. Murray. 534 pages, 160 illustrations. Buenos Aires: Editorial Bibliográfica Argentina, 1956.

[3]CLINICAL UROLOGY. By Oswald Swinney Lowsley, A.B., M.D., F.A.C.S., F.I.C.S., and Thomas Joseph Kirwin, M.A., M.S., M.D., F.A.C.S., F.I.C.S. Drawings by William P. Didusch. 3rd ed. Vols. I and II. 985 pages, 599 illustrations. $32.50 per 2 volume set. Baltimore: The Williams & Wilkins Co., 1956.

understand some of the principles of renal physiology and acid-base balance that always have been hazy in his mind. The final chapter on chemotherapy and antibiotics in urology is well conceived and well executed. It presents an excellent summary of the basic problems of bacterial sensitivity and resistance, as well as the mode of action and effectiveness of the available drugs and antibiotics. All in all, the book is well done and can be recommended as a valuable addition to any urologic library.

—*John L. Emmett.*

A VAST EXPERIENCE as a pioneer and teacher is culminated in Sterling Bunnell's third edition[4] of his classic work. Probably no single surgical volume contributed more to extremity reconstruction during World War II than his *Surgery of the Hand* and his untiring personal effort to develop a group of surgeons who could carry his principles back into the field of civilian injuries where the problems are as great as those encountered during wartime.

Although the format of the original text remains, the scope has been expanded through case studies and further clarification of anatomic, functional, and surgical principles. Chapter IV, as in the past, is of special importance for it gives the philosophy necessary for successful reconstructive surgery. The bibliography is exhaustive and up to date.

Bunnell's original work on ischemic intrinsic muscle contracture has been fully developed and has led to a better understanding of rheumatic deformities. Valuable hand function can be restored to these pitifully disabled hands through appropriate intrinsic tenectomies and arthrodeses. This phase of hand surgery is open for further exploration.

A single gig pull-out traction wire suture is illustrated for primary tendon repairs. Tendon transfers, so often needed to compensate for the intrinsic muscle paralysis following median and ulnar nerve disruption, have been carefully worked out by Bunnell. These transfers, so helpful in restoring function to the many with peripheral nerve injuries during the war, have now been applied to the "claw" hand deformity of lepers, both in this country and in India. The thumb reconstruction problem is realistically covered together with more recent methods of neurovascular tissue transfers.

Restoration of useful function to the severely disabled hand requires time and skill; Bunnell's great work is a gift of experience to those interested in this important field of surgery. —*J. William Littler.*

[4]SURGERY OF THE HAND. By Sterling Bunnell, M.D. 3rd ed. 1,079 pages, 1,047 illustrations and 9 color plates. $22.50. Philadelphia and Montreal: J. B. Lippincott Co., 1956.

BOOKS RECEIVED

BOOKS received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

WOMEN DOCTORS OF THE WORLD. By Esther Pohl Lovejoy, M.D., LL.D., D.P.H.(Hon.). 413 pages, 50 illustrations. $5.95. New York: The Macmillan Co., 1957.

PRINCIPLES OF UROLOGY; AN INTRODUCTORY TEXTBOOK TO THE DISEASES OF THE UROGENITAL TRACT. By Meredith F. Campbell, M.S., M.D., F.A.C.S. 622 pages, 319 illustrations. $9.50. Philadelphia and London: W. B. Saunders Co., 1957.

ATLAS OF GASTROENTEROLOGICAL CYTODIAGNOSIS. By Prof. Dr. med. N. Henning and Priv.-Doz. Dr. med. S. Witte. English translation by Dr. R. O. K. Schade. 103 pages, 114 illustrations. DM 38. Stuttgart: Georg Thieme Verlag, 1957.

CHIRURGIE DU PANCRÉAS. By Lucien Leger and Jacques Bréhant. 504 pages, 154 illustrations. 4.800 fr. Paris: Masson et Cie, Éditeurs, 1956.

MENSCHLICHE UND TIERISCHE GEWEBSTHROMBOKINASEN. By Dr. H. A. Thies. 56 pages, 12 illustrations. $2.85. Stuttgart: Georg Thieme Verlag, 1957.

THE MANAGEMENT OF ABDOMINAL OPERATIONS. Edited by Rodney Maingot, F.R.C.S. 2nd ed., in 2 volumes. Vol. I, 772 pages, 640 illustrations in 414 figures. Vol. II, 554 pages, 640 illustrations in 444 figures. New York: The Macmillan Co., 1957.

LA GASTRECTOMIE POUR ULCÈRE. By R. de Vernejoul, E. Henry, and R. Devin. 210 pages, 96 illustrations. 3.000 fr. Paris: Masson et Cie, Éditeurs, 1956.

CLINICAL USE OF RADIOISOTOPES; A MANUAL OF TECHNIQUE. Edited by Theodore Fields, M.S., F.A.C.R. (Assoc.), and Lindon Seed, M.D. 455 pages, illustrated. $9.50. Chicago: The Year Book Publishers, Inc., 1957.

SURGERY: PRINCIPLES AND PRACTICE. Edited by J. Garrott Allen, M.D., Henry N. Harkins, M.D., Ph.D., Carl A. Moyer, M.D., and Jonathan E. Rhoads, M.D., D. Sc.(Med.). 1495 pages, 623 illustrations. $16.00. Philadelphia and Montreal: J. B. Lippincott Co., 1957.

THE ESSENTIALS OF MODERN SURGERY. Edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and Sir Arthur E. Porritt, K.C.M.G., C.B.E., M.A., M.Ch., F.R.C.S. 5th ed. 1276 pages, 649 illustrations, many in color. Edinburgh and London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1957.

SPINAL CORD COMPRESSION; MECHANISM OF PARALYSIS AND TREATMENT. By I. M. Tarlov, M.D. 147 pages, 41 illustrations. $7.50. Springfield, Ill.: Charles C Thomas, Publishers, 1957.

1957 MEDICAL PROGRESS; A REVIEW OF MEDICAL ADVANCES DURING 1956. Editor, Morris Fisbbein, M.D. 367 pages, not illustrated. $6.00. New York, Toronto and London: The Blakiston Division, McGraw-Hill Book Co., Inc., 1957.

DIE PROGNOSE DER WIRBELSAEULENLEIDEN; EINE BERUFSPROPHYLAKTISCHE BETRACHTUNG. By Prof. Dr. J. E. W. Brocher. 67 pages, 33 illustrations. DM 12.80. Stuttgart: Georg Thieme Verlag, 1957.

THE METABOLIC RESPONSE TO NEONATAL SURGERY. By P. P. Rickham, M.S.(Lond.), F.R.C.S., D.C.H. 93 pages, illustrated. $5.00. Published for The Commonwealth Fund. Cambridge, Mass.: Harvard University Press, 1957.

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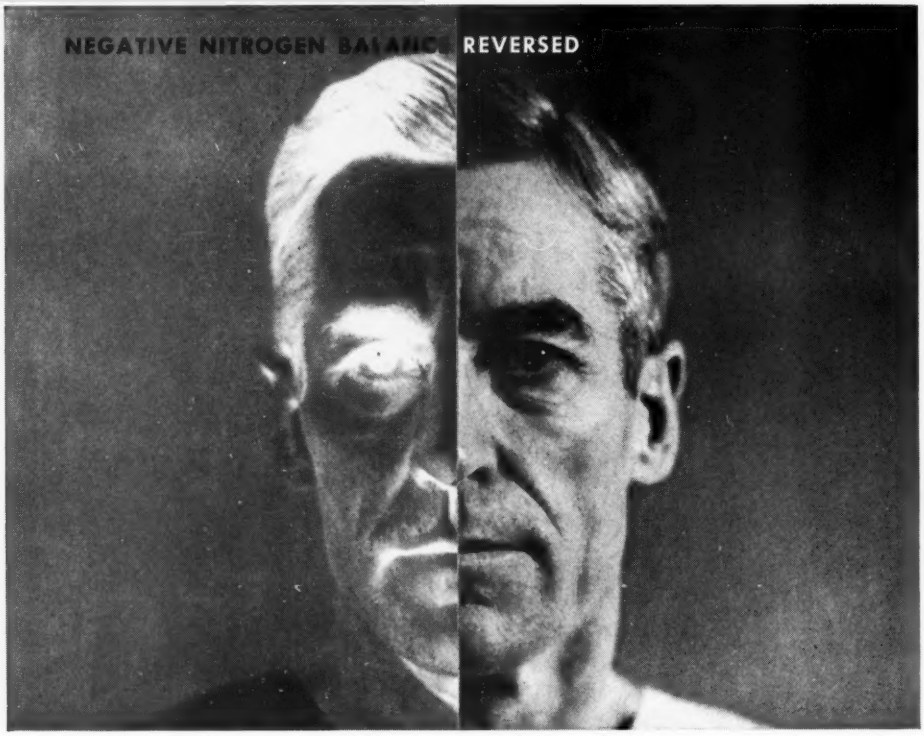

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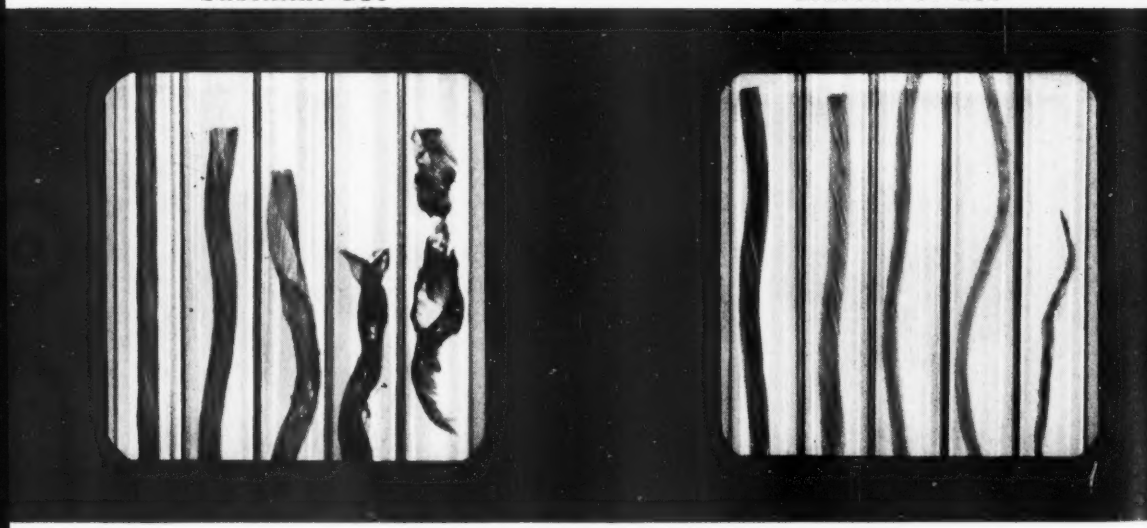

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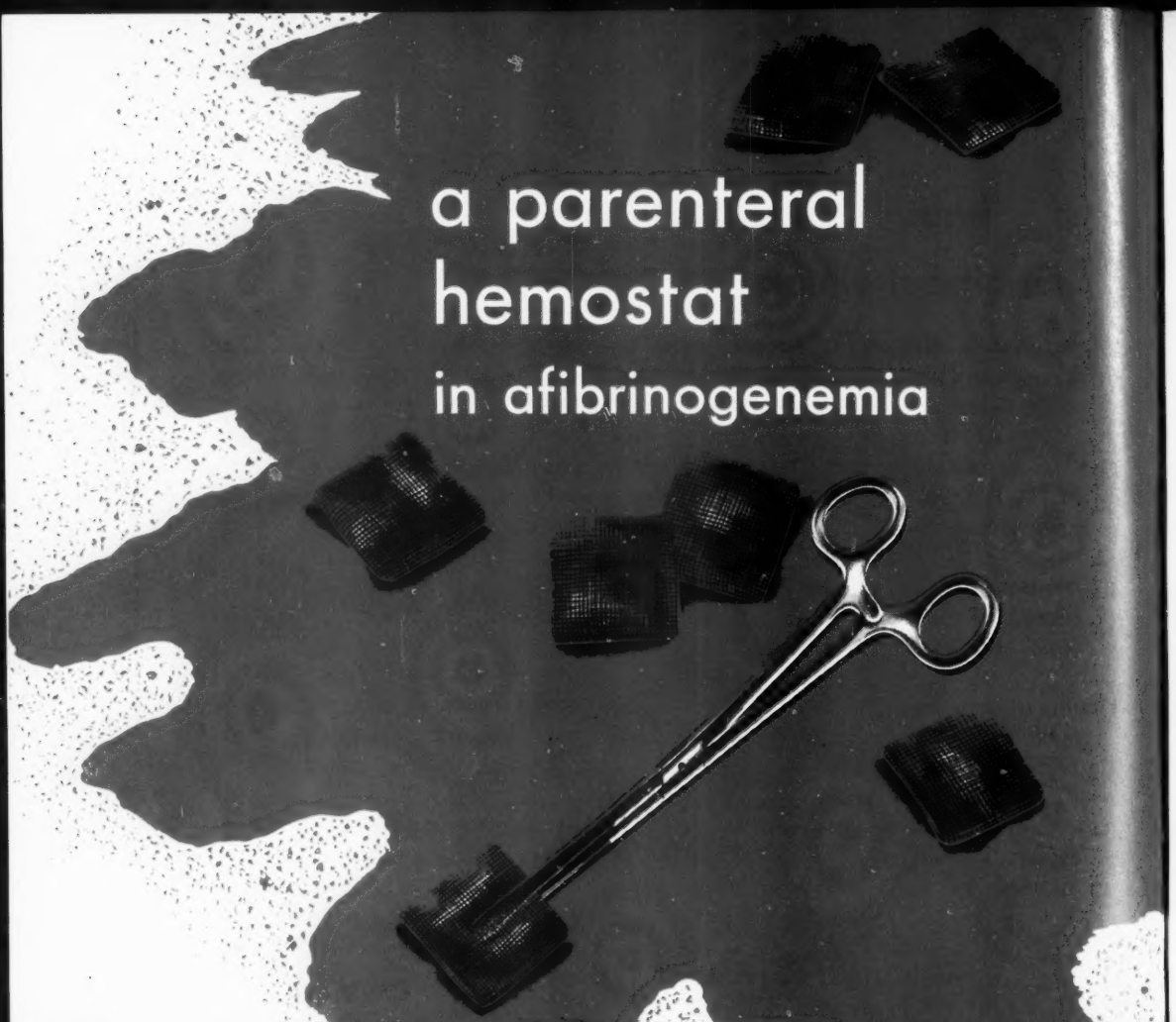

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(1) Compilation of investigative studies, Schering Corporation.
(2) Department of Pharmacology, Schering Corporation.
(3) Ayd, F. J., Jr.: J. Am. Geriatrics Soc. *5*:92, 1957.

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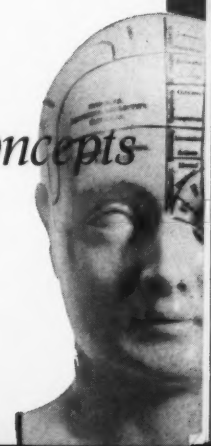

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1. Miller, J. M.; Surmonte, J. A.; Ginsberg, M., and Ablondi, F. B.: Postgraduate Medicine 20:260 (Sept.) 1956.

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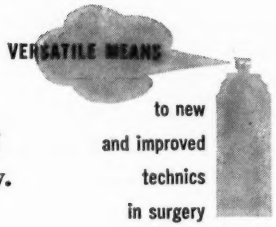

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Iron Deficiency Anemia of Infancy: IMFERON provides a convenient safe means for restoring hemoglobin levels and iron reserves in anemic infants. Excellent results were obtained by Gaisford and Jennison[2] with IMFERON in 100 iron-deficient infants. From a pretreatment average of 54.5 per cent, hemoglobin levels rose to 87 per cent 10 weeks after the start of therapy. Clinical improvement paralleled this response. Premature infants and surgical cases were similarly benefited. IMFERON gave "...all the advantages of transfusion or intravenous therapy without the disadvantages."[2] There were no side effects in any of the infants treated. Wallerstein[3] confirmed these results, furnishing evidence that IMFERON is well absorbed and appears in the bone marrow 12 to 24 hours after injection. Results are equal to those with intravenous saccharated iron oxide without the unpleasant side effects. Sturgeon[4] showed that the first year's iron requirements in infancy can be supplied with three injections of IMFERON.

Iron Deficiency Anemia of Pregnancy: Nausea precludes oral iron therapy in many anemic pregnant women. In those with severe anemia who are first seen late in pregnancy, prompt hemoglobin regeneration is unobtainable with oral iron. IMFERON produced prompt hemoglobin responses in anemia of pregnancy,[5,6] the results being similar to those obtained with intravenous saccharated iron oxide. Side effects were virtually absent with IMFERON.[5,6]

Resistant Hypochromic Anemia: Patients who do not respond to oral iron, those who cannot take oral iron and those with gastrointestinal pathology respond well to injections of IMFERON.[7-11] While oral iron is of little value in treating the anemia of rheumatoid arthritis, IMFERON is "...as beneficial as intravenous iron and easier to administer."[9]

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References: (1) Brown, E. B., and Moore, C. V., in Tocantins, L. M.: Progress in Hematology, New York, Grune & Stratton, Inc., 1956, vol. I, p. 25. (2) Gaisford, W., and Jennison, R. F.: Brit. M. J. 2:700 (Sept. 17) 1955. (3) Wallerstein, R. O.: J. Pediat. *49*:173, 1956. (4) Sturgeon, P.: Pediatrics *18*:267, 1956. (5) Jennison, R. F., and Ellis, H. R.: Lancet *2*:1245 (Dec. 18) 1954. (6) Scott, J. M., and Govan, A. D. T.: Brit. M. J. *2*:1257 (Nov. 27) 1954. (7) Grunberg, A., and Blair, J. L.: A.M.A. Arch. Int. Med. *96*:731, 1955. (8) Millard, J. B., and Barber, H. S.: Ann. Rheumat. Dis. *15*:51, 1956. (9) Baird, I. M., and Podmore, D. A.: Lancet *2*:942 (Nov. 6) 1954. (10) Cappell, D. F.; Hutchinson, H. E.; Hendry, E. B., and Conway, H.: Brit. M. J. *2*:1255 (Nov. 27) 1954. (11) Stevens, A. R.: A.M.A. Arch. Int. Med. *96*:550 1956.

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Zanchol has proved useful in preventing obstruction of T tubes and bile duct prostheses by sediment, and for the long-term management of patients whose gallbladders have been removed or for those who require reconstructive surgery of the common duct.

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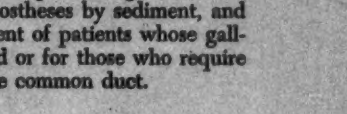
Zanchol is a synthetic fluoranthene derivative with a ketobutyric acid side chain. Unlike bile salts and bile acids it does not have a steroid structure. The formula is:



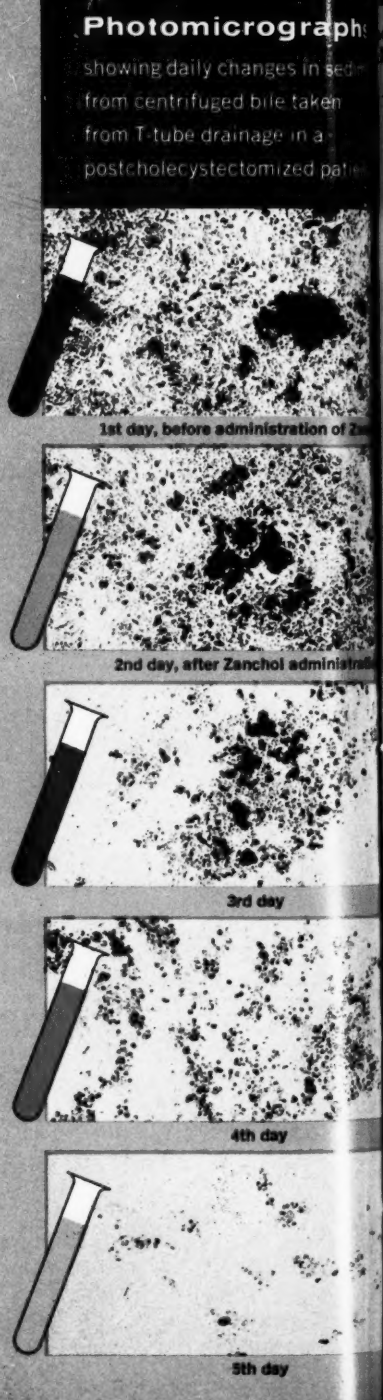
True long-action t

2 1

Improved abstergence and color change in bile produced by Zanchol. Tube No. 1, with light colored bile, considerable sediment and clouding, was from T-tube bile in a postcholecystectomized patient. Very little foam was obtained on shaking. Tube No. 2 contains bile from the same patient one day after the administration of Zanchol. The color is better, less sediment is present and the bile has greater clarity. The larger amount of foam obtained by shaking lasts for a longer period of time.

Photomicrograph

showing daily changes in sed
from centrifuged bile taken
from T-tube drainage in a
postcholecystectomized pat



new biliary abstergent

linical applications of Zanchol

e improvement in bile secretion provided by Zanchol ficates its use in the following conditions:

After all biliary operations[1] to prevent the postcholecystectomy syndrome.

Routine use of Zanchol usually clears up the symptoms of eructation and abdominal pain or discomfort frequently occurring after cholecystectomy. Administration of Zanchol with meals provides an additional bile flow, thus partially compensating for the absence of a bile reservoir. Barowsky[2] observed that Zanchol often relieves postcholecystectomy distress of several years' duration.

In postcholecystectomized patients with T-tube drainage.

Bilirubin sediment precipitates in T tubes and frequently obstructs bile flow. Removal of solids from the bile by the administration of Zanchol keeps T tubes free from sediment and encrustation. McGowan[1] states:

"After the first few patients had received this preparation, its usefulness was so obvious that it was prescribed routinely for all patients operated upon for gallbladder disease in whom it was necessary to place a T tube in the common bile duct for prolonged biliary drainage....

"It has long been a known fact among doctors doing biliary surgery that tubes become covered and often plugged with orange colored sediment of bilirubin after a sojourn in the common duct and that a prosthesis, such as a rubber or metal tube, put into the duct to replace a destroyed portion of the duct invariably becomes plugged and reoperation is required. From this study, it is safe to conclude that such patients could be benefited indefinitely by the administration of SC-1674 [Zanchol]."

In chronic cholecystitis when surgery is not employed.

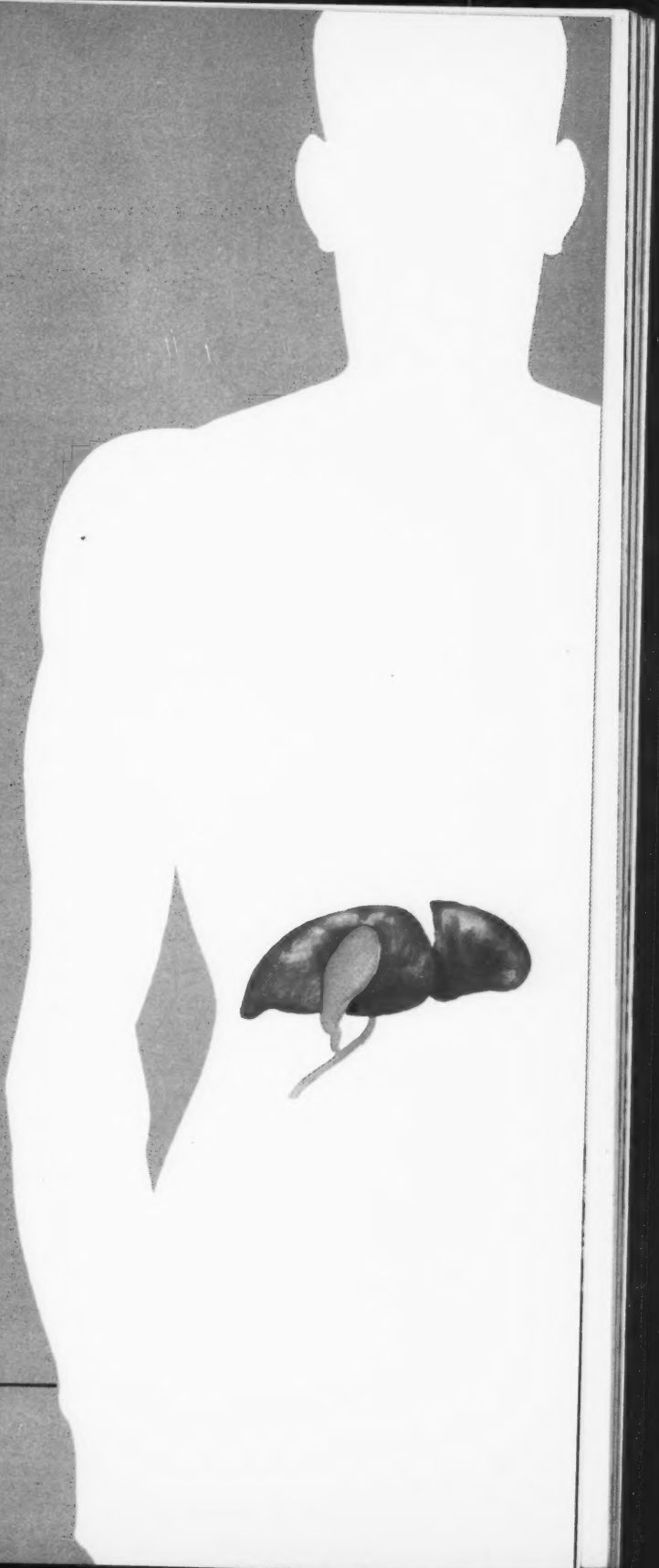
Patients with chronic cholecystitis who are not considered good candidates for cholecystectomy will receive symptomatic relief from the administration of Zanchol.

The usual daily dosage is three or four tablets with eals and at bedtime.

Zanchol is available as tablets of 250 mg. each in ottles of 100 and 1,000.

McGow n, J. M.: Clinical Significance of Changes in Common Duct Bile Resulting from New Synthetic Choleretic, Surg., Gynec. & Obst. 103:163 (Aug.) 1956.

Barow y, H.: A Clinical Evaluation of the Choleretic Effect of a Synthetic metic ato Acid, SC-1674, to be published.



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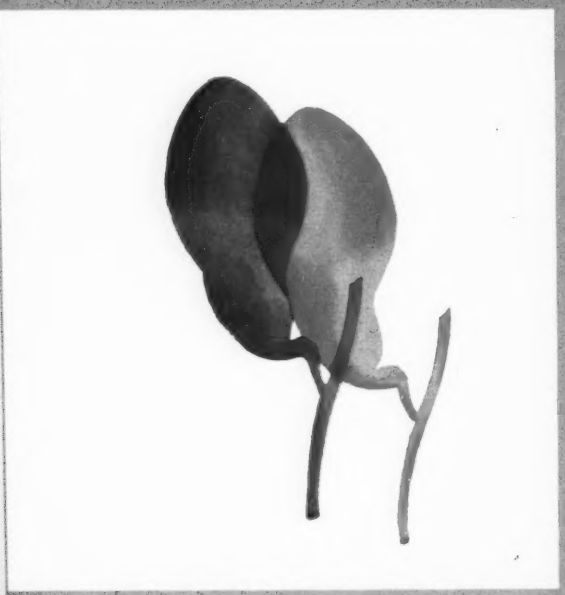

ZANCHOL

Pharmacologic action in man

Direct observation[1] in cholecystectomized patients with T tubes in the common duct showed that Zanchol produced the following effects:

Bile Color Was Improved

In every patient the bile changed to a brilliant deep green, regardless of its original color.

Bile Sediment Disappeared

The sediment in biliary drainage fluid disappeared in five to ten days. Bilirubin and other slightly soluble material were dissolved.

Bacterial Content Decreased

After Zanchol was given there were no putrid odors in most bile specimens when allowed to stand at room temperature. Motile bacteria were reduced in number or were absent. However, since laboratory studies indicate that Zanchol has no bacteriostatic activity, this observation is probably the result of increased flow of bile and reduction of sediment and debris produced by Zanchol.

Volume and Fluidity Increased

A progressive increase in the amount of bile flow was noted. Viscosity was lowered and the bile appeared to flow more readily through the common duct.

Bile Abstergence Augmented

A definite abstergent action was observed in all patients. More foam was produced on shaking and the froth lasted for a longer period in bile specimens from Zanchol-treated patients.

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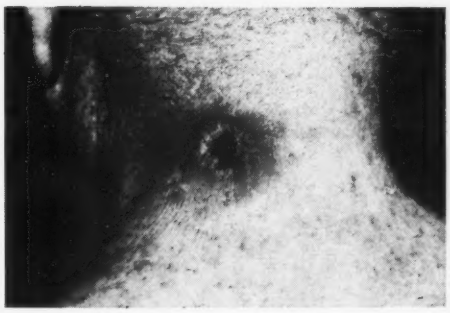
Right: Lesion almost healed after two weeks of therapy with PANAFIL. Complete healing one week later.



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References: (1) Miller, E. W.: New York J. Med. *56*:1446, 1956. (2) Garnes, A. L., and Barnard, R. D.: Angiology *8*:13, 1957. (3) Morrison, J. E., and Casali, J. L.: Am. J. Surg. *93*:446, 1957. (4) Wood, O. H.: Maryland M. J., in press.

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. . . TO GET TO SURGERY

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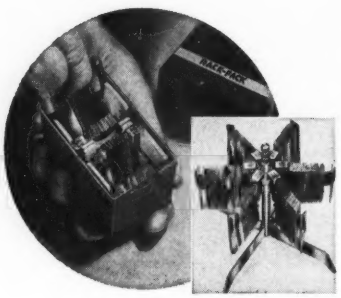
DETACHABLE SURGICAL BLADES

must 'survive' a rigid series of progressive scientific tests to qualify as suitable for surgical use. Those that 'pass' are surgically perfect and uniformly sharp throughout their entire cutting edge. They will remain sharp and useful for longer periods . . . an important factor in economy when yearly volume of purchases is considered.



Specify RACK-PACK® packages in ordering gross and half gross quantities . . . eliminating unwrapping —handling—racking of individual blades. A time and labor saver for the O.R. personnel.

It's Sharp

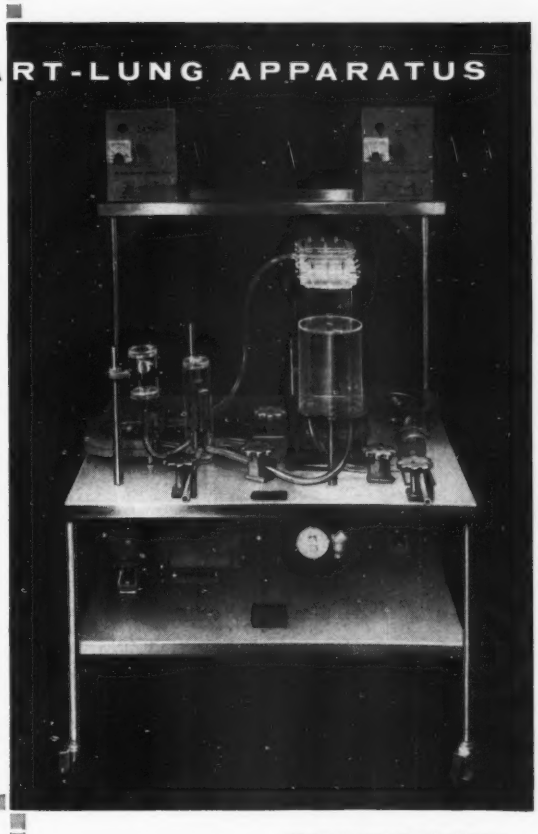
Ask your dealer

BARD-PARKER COMPANY, INC.
Danbury **Connecticut, U.S.A.**

NEW *MARK* MEDICAL INSTRUMENTS

MARK G-K HEART-LUNG APPARATUS

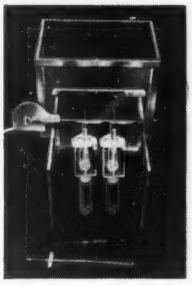
Maintains cardiorespiratory functions over 60 minutes



This Gibbon Type Apparatus for maintenance of extra-corporeal cardiorespiratory functions has been thoroughly proven in a substantial number of operations for the correction of congenital and acquired abnormalities of the heart. It was developed through more than five years of intensive study by many research groups including the National Heart Institute.

Mark G-K Heart-Lung Apparatus maintains high flow rates (up to 5000 cc/min.) at a constant rate without bubbles or destruction of clotting constituents . . . during perfusion period system is balanced by regulating only one pump . . . utilizes DeBakey non-occlusive pumps . . . explosion-proof construction.

The Mark Volumetric Respirometer



The new Mark Volumetric Respirometer performs plasma CO_2 determinations to within ± 0.3 mM per liter of known values (2%). Operation is simple and a single technician can make 24 to 32 determinations in one hour (large unit).

Mark Heart Defibrillator

Provides one-switch control of both voltage and duration of shock. Three pre-set choices of pulse amplitude and duration: 280 volts for 1/20 second; 220 volts at 1/10 second; 130 volts at 1/4 second. Pulse current: 1.5 to 3 amp. Requires no warm-up; circuit-breaker eliminates fuse changing. The only commercially available defibrillator that meets explosion-proof standards of hospitals.

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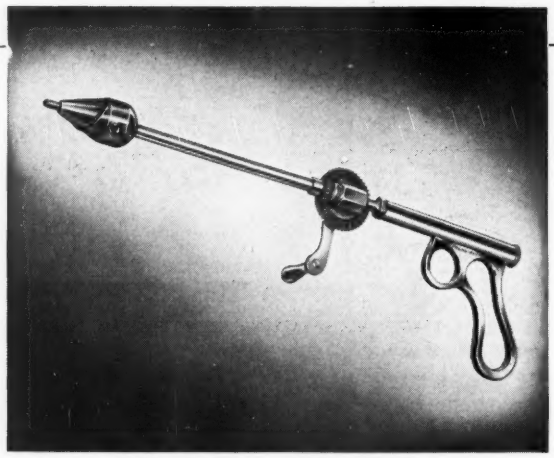
BOOTH B22, AMERICAN MEDICAL ASSOCIATION CONVENTION
NEW YORK, JUNE 3-7

ULLERY CONIZING BIOPSY KNIFE*



Designed by JOHN C. ULLERY, M.D., Columbus, Ohio

*Patent Pending

BIOPSY SPECIMENS WITH IN-VIVO CHARACTERISTICS

This new knife removes uterine cervix tissue for biopsy or for certain gynecologic conditions, replacing the scalpel-and-loop technic.

The pathologist receives superior specimens for microscopic examination—with no charring or destruction of cellular structure.

A continuous circular biopsy is made of the entire outer surface of the cervix as well as the endocervix by the conical spiral cutting knife. The design of the blade forces the biopsy specimen into the interior cavity of the instrument where it is preserved. Any pathologic areas are cut out at the same time that the specimen is removed.

After the operation is complete, the parts of the instrument are separated and the specimen is removed in as good condition as it was *in vivo*. The pathologist therefore receives a more complete and representative specimen and can make a more accurate final diagnosis.

THIS INSTRUMENT IS AVAILABLE ONLY FROM PILLING—ORDER DIRECT

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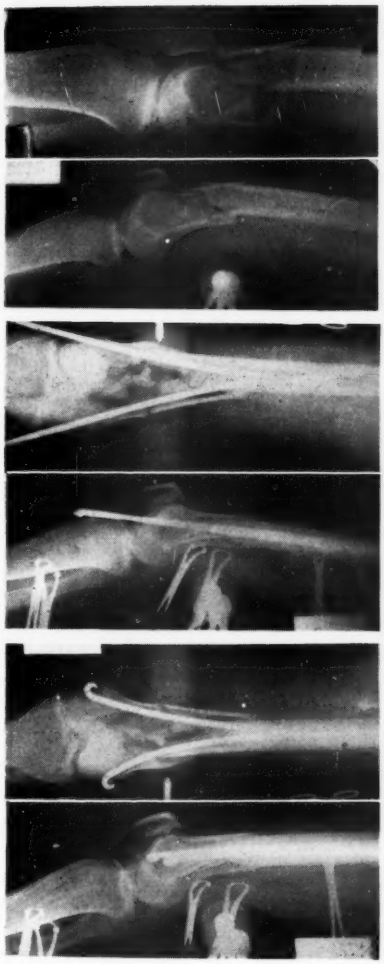
CABLE ADDRESS: Surgical-Phila.

The RUSH COUNTERSUPPORT



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The RUSH® MEDULLARY PIN
PAT No. 2 579,968

FOR FRACTURES OF FEMUR
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Simplifies Pinning By:

- RELAXING MUSCLE PULL
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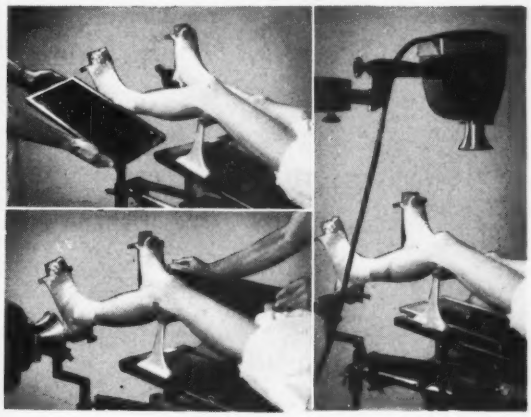
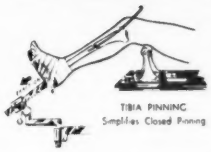
- ALLOWING STERILE FIELD
- PERMITTING X-RAYS DURING PROCEDURE



X-Rays shown are actual operating room films showing technic of CLOSED PINNING of comminuted supra-condylar fracture of femur in elderly female. Note shadow of RUSH COUNTERSUPPORT.



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YOU GET THESE BALANCED PROPERTIES IN EVERY GRADE OF NEW CURITY ADHESIVE

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No. 1 of an operative series—for details, see next page

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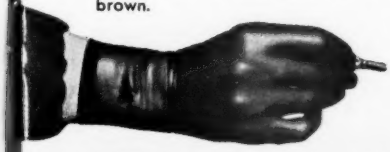
Brown Milled Surgeons' Gloves by SEAMLESS

'LIMBER-LATEX'—the softest, most comfortable of all latex gloves—in white or brown.



'CREST'—the thinnest, most sensitive surgeon's glove available—for special surgery.

Maximum tactile sensitivity assures unmatched "sightless seeing."

Minimal radial bind provides maximum hand comfort.

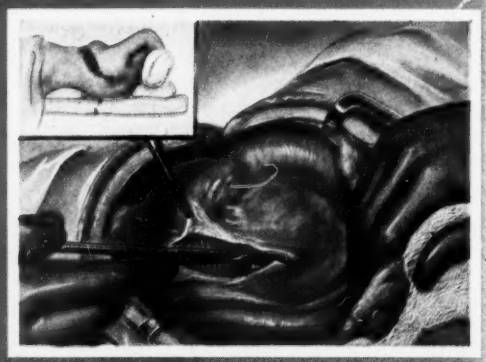
Non-skid surface affords more positive handling when wet.

Hypoallergenic properties minimize the possibility of contact dermatitis.

No. 1 in professional preference because they are No. 1 in surgical performance

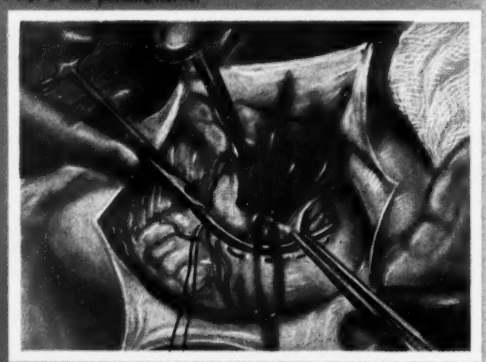
KEY ADVANCES IN OPERATIVE TECHNICS* — *Mitral Commisurotomy*[1]

1. Lateral postero-anterior view of heart, showing greatly dilated left auricle and calcified, thickened mitral valve. Inset shows typical narrowing of valve viewed from above.

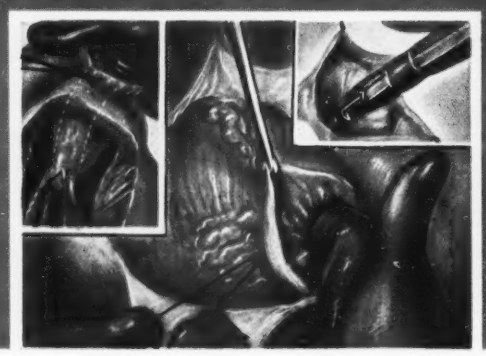


2. Postero-lateral pericardial incision. Enlargement of left ventricle and pulmonary artery is evident. Dilated left auricle presses on esophagus. Pericardium is being incised just posterior to the phrenic nerve.

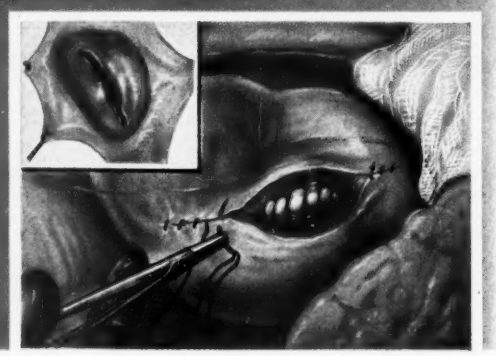
3. A purse string suture is placed around the auricular appendage. This suture is carefully started just above the circumflex artery.



4. A clamp placed just above the suture line is released slightly allowing a gush of blood to wash away any accumulated thrombotic material. Purse string suture is then tightened.



5. Finger is inserted into auricle. Inset (left) shows finger about to dilate valve. Inset (right) depicts alternate procedure with guillotine knife fastened to finger for rigid valve.



6. The auricular appendage is closed by means of the purse string and a whipstich suture. The pericardium is left partially open. Inset shows an adequate commisurotomy.

Mitral commisurotomy is one of a series of surgical drawings in color illustrating important new operations successfully perfected during the past decade. It is brought to you as a service by Seamless, the world's largest manufacturer of surgeons' gloves. If you would care to examine any of the Seamless Gloves . . . Brown Milled, White or Brown 'Limber-Latex', or the new 'Crest' for eye, brain or heart surgery, write for a sample giving your glove size.

**Based on an opinion survey of 2,500 general surgeons.*

1. Glover, R.P., *International Symposium on Cardiovascular Surgery*, Edited by Conrad R. Lam, (Philadelphia: W. B. Saunders Company, 1955), pp. 179-211.

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"So then I told the doctor...
"Why do you have such an unwholesome attitude toward watercress and sal*tines*? You simply cannot *expect* the girls in the Henry Hudson Fowl Protection League to eat big, *heavy*, fattening *meals* . . ."

When you finally bring her around, remember that what she'll probably need first . . . and *most* . . . is the essential B-complex. And that's a good time for

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Thiamine Mononitrate	6 mg.
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Ascorbic Acid	150 mg.
Desiccated Liver, N. F.	300 mg.
Brewer's Yeast, Dried	150 mg.

As a dietary supplement: 1 or 2 tablets daily
In convalescence: 2 or more daily

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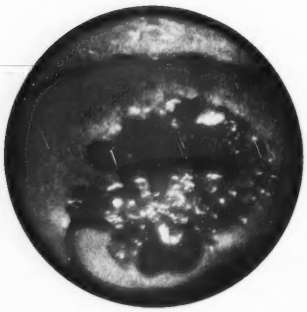

Pre-cauterization

2 weeks post-cauterization

3 weeks post-cauterization,
healing nearly complete

PHOTOGRAPHS BY SCHWARTZ, J.: AM. J. OBST. 63:579, 1952

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FORMULA: 0.2% FURACIN in water-miscible base; hermetically sealed in yellow foil.

*Schwartz, J., and Nardiello, V.: Am. J. Obst. 65:1069, 1953.

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a new class of antimicrobials—neither antibiotics nor sulfonamides

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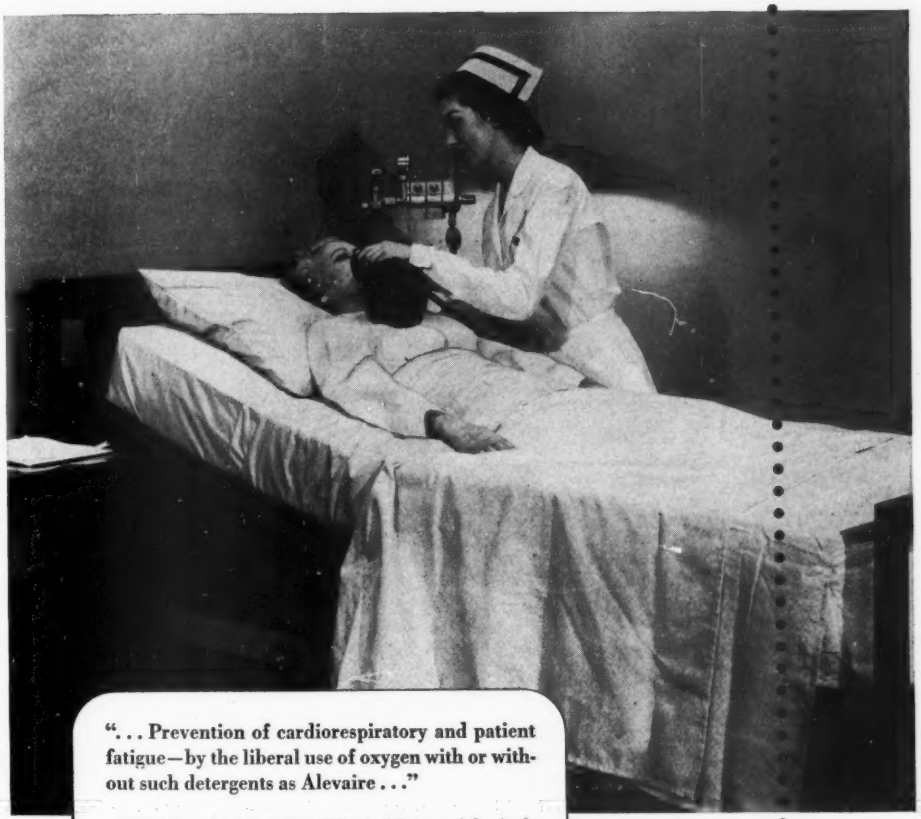
In abdominal surgery of the aged..... O_2



"... Prevention of cardiorespiratory and patient fatigue—by the liberal use of oxygen with or without such detergents as Alevaire ..."

—*Principles and Safeguards in Abdominal Surgery of the Aged:* Journal of the American Medical Association, Vol. 160, No. 16, pages 1375-1378; Richard K. Gilchrist, MD, and Frederick H. dePeyster, MD; Chicago.

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References: 1. Gamble, J.R., et al. Arch. Int. Med. 95:52, 1955. 2. Gamble, J.R., et al. J. Lab. & Clin. Med. 42:805, 1953.

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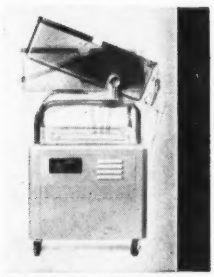
DIVISION OF MERCK & CO., INC. PHILADELPHIA 1, PA.

The Rockette bassinet is of seamless, stainless steel—easily cleaned and sterilized. Full-length piano hinge gives sturdy support to the metal-bound, shatterproof glass lid.

Comfortable working height of the Rockette facilitates care, and safety glass lid permits observation of visceral excursions and changes of skin color during treatment of neonatal asphyxia.

IN NEONATAL ASPHYXIA:

Natural, non-traumatic resuscitation



Rocking provides gentle, non-traumatic activation of the inert diaphragm through alternate excursions of the viscera. Rocking likewise gently stimulates circulation, aids oxygenation of the vital higher centers, until normal respiration is established.

The ROCKETTE® is the only commercially-available, fully automatic rocking bassinet. Explosion-proof,* simple to operate, and ruggedly built, the ROCKETTE requires no attention while in operation, and minimal maintenance. Both the angle and the rate of rocking are easily adjustable.

"Since," as Millen[1] states, "the most effective aid to respiration must help both circulation and ventilation and . . . ventilation has both an inspiration and expiration phase,[2] only Eve's rocking method of resuscitation will do all this."[3] Millen tells how this method reversed cyanosis and maintained respiration in two infants who required 11 and 45 minutes, respectively, to start breathing spontaneously.[1]

The ROCKETTE rocking resuscitator may be purchased with 30-day return privilege, express collect. To obtain 8-10 minute ROCKETTE film, or to place your return-privilege order, phone us collect (OSborne 5-5200, Hatboro, Pa.)

*Listed by Underwriters' Laboratories for use in hazardous locations.

References: (1) Millen, R. S.: N.Y. State J. Med. 55:779, 1955.
(2) Karpovitch, P.: Adventures in Artificial Respiration, New York, Associated Press, 1953.
(3) Eve, F. C.: Lancet 2:995 (1932); Eve, F. C., and Forsyth, N. C.: Brit. M. J. 2:554 (1948).

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Millen-Davies Rocker

An ingenious vaporizer-aspirator assembly provides the Rockette with a steady flow of humidified oxygen, with mild suction available for aspiration during rocking.

for simple, non-traumatic management of neonatal asphyxia

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Makers of the **Isolette®** infant incubator, the **Croupette®** cool vapor tent, the **Hydrojette®** mobile humidifier-aspirator, and the **Jefferson Ventilator.***

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A bifurcated Edwards-Tapp A-G™ Tube is now available. The upper part has a lumen of ⅝″ and is 5 inches long. The limbs have a lumen of ⅜″ and are 9½ inches long. These limbs are crimped to allow flexing without kinking, so that this graft can be used as a by-pass as well as a replacement graft.

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buffers acid
builds tissue
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provides a bland high protein diet

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a peptic ulcer patient...

comfortable...well fed...**on the job!**

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for safe pressure infusion...just squeeze it!

safe, dependable infusion system

pressure administration without air embolism

flexible plastic Blood-Pack® infusion unit permits application of manual or mechanical pressure—closed system eliminates hazards of air embolism

no stoppage—no slowdown

- superior collection unit—Blood-Pack® system hemorepellant plastic surfaces curb sludging and clotting
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Not a "caine" derivative. Good relief was provided in more than 15,600 case studies. Sensitization was negligible, and neither toxicity nor cross-sensitization was observed. Abbott

LOCAL ESTROGEN APPLICATION GREATLY SIMPLIFIES TREATMENT OF SENILE VAGINITIS

THIS method provides an "almost immediate healing and soothing effect" Doyle reports,[1] and "is a valuable therapeutic constituent in the management of vaginitis and vaginal infections, regardless of etiology."[2] This worker employed "Premarin" Vaginal Cream applied locally and found it "superior" to the use of suppositories. There were none of the "side-effects frequently noted with synthetic products..."[1]

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1. Doyle, J. C.: California Med. *71*:15 (July) 1949. • 2. Doyle, J. C.: Urol. & Cutan. Rev. *55*:618 (Oct.) 1951. • 3. Hamblen, E. C., in Stieglitz, E. J.: Geriatric Medicine, ed. 2. Philadelphia, W. B. Saunders Company, 1949, p. 657.

"Premarin" Vaginal Cream

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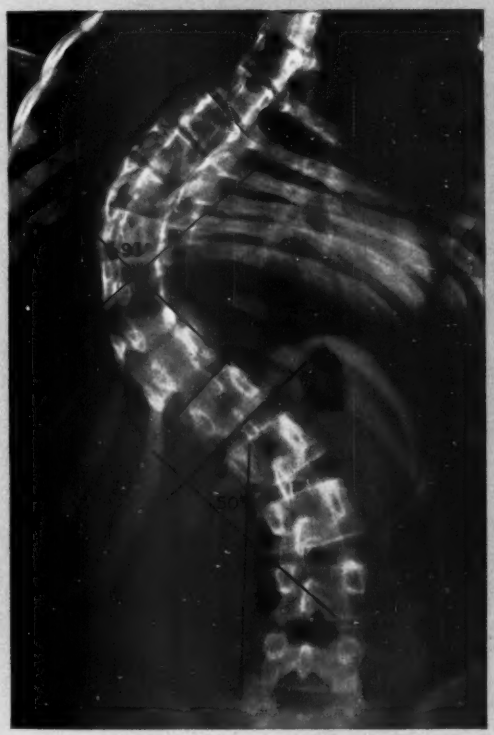
Radiographs and photographs like these

are invaluable—to the attending physician—to teachers and students!



1. CASE: 14-year-old girl with idiopathic scoliosis. Precorrection radiograph with patient seated.

2. Postcorrection radiograph with patient in plaster jacket following spinal fusion (top and bottom of the fusion marked by metallic clips).

3. Right dorsal curve has been corrected in plaster turnbuckle jacket and back is seen exposed through window. Methylene blue tattoo marks identify area of vertebral column to be fused. *Steps in surgery shown on page following.*

Here you see a trend. With the visual data reproduced on these pages, the physician can review his case, discuss it in detail with associates and students.

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4. Posterior elements of the vertebrae to be fused have been exposed by subperiosteal dissection.

5. Interdigitation of bony spicules across the interlaminal spaces has been completed.

6. Raw bony area is reinforced by slivers of cancellous bone obtained from the bone bank.

7. Incision closed.

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Treat stress by specific vitamin repletion

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FORMULATED UNDER RIGID QUALITY CONTROL FOR YOUR PRESCRIPTION NEEDS

STRESSCAPS replenish the specific water-soluble vitamin losses sustained by patients under such stress situations as surgery, burns, fractures, trauma or shock.

The STRESSCAPS formulation is based on the most recent knowledge regarding the vitamin requirements of the human body under stress.

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Thiamine Mononitrate (B_1)	10 mg.
Riboflavin (B_2)	10 mg.
Niacinamide	100 mg.
Ascorbic Acid (C)	300 mg.
Pyridoxine HCl (B_6)	2 mg.
Vitamin B_{12}	4 mcgm.
Folic Acid	1.5 mg.
Calcium Pantothenate	20 mg.
Vitamin K (Menadione)	2 mg.

Average Dose: 1-2 capsules daily.

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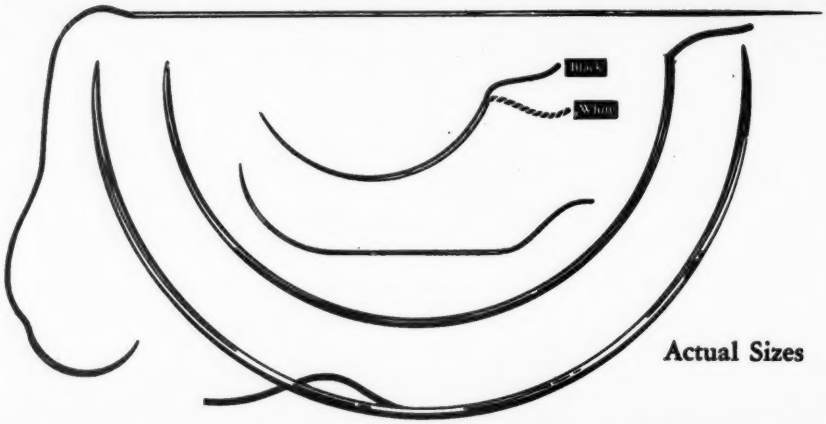
for your *specialized* techniques— specify Deknatel



Actual Sizes

Deknatel stainless steel needles are manufactured in our own plant. The Deknatel Research Staff can make *any* desired needle to your specifications.

for your *routine* techniques— specify Deknatel

COMPARE...

SAMPLES SENT UPON REQUEST.
All needles available on Deknatel's complete line of sutures.

I would like to compare Deknatel with my present needle:

_____
(Description)

_____

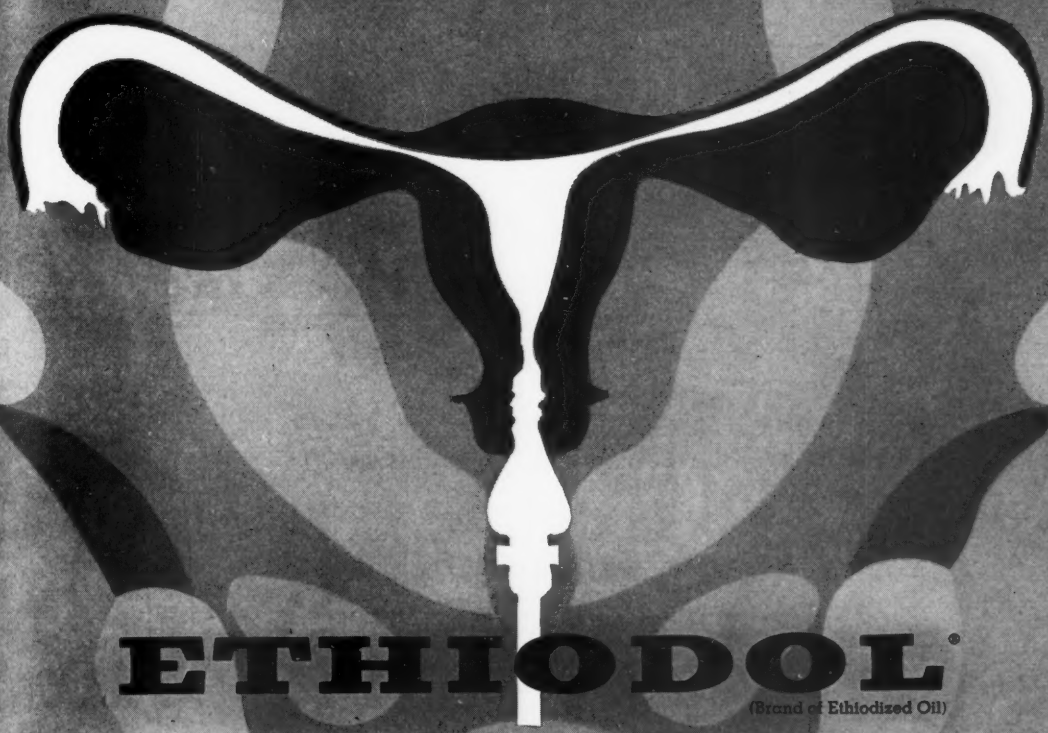
NAME _____

ADDRESS _____

CITY **ZONE** **STATE**

J. A. DEKNATEL & SON, Inc.
Queens Village 29, New York

the advantages you want in hysterosalpingography...



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(Brand of Ethiodized Oil)

LIPIODOL® diagnostic with free-flowing viscosity

low viscosity for easier administration and free passage through narrow or strictured tubes or openings.

excellent radiopacity provides films as clear as with LIPIODOL for dependable diagnosis.

optimal absorption—completely absorbed usually within 45 days. Permits 24-hour film.

minimal patient discomfort—painless on contact with peritoneum. Bland, nontoxic and nonirritating.

ETHIODOL, brand of ethiodized oil, is the ethyl ester of the iodinated fatty acid of poppyseed oil, containing 37% iodine. Available in 10-cc. ampules, boxes of two. A development of Guerbet Laboratories.

Literature available upon request.

FOUGERA E. FOUGERA & COMPANY, INC • 75 Varick Street, New York 13, N. Y.

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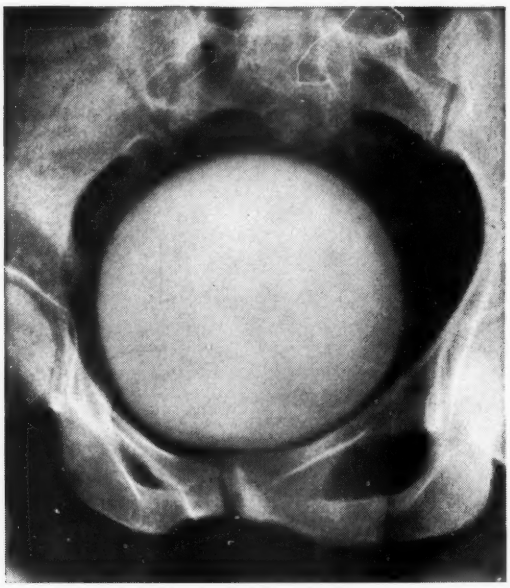

Relieves postpartum retention aseptically

URECHOLINE®

CHLORIDE

(BETHANECHOL CHLORIDE)

URECHOLINE offers worthwhile therapeutic and psychologic advantages in managing urinary retention. In one study[1], prophylactic administration of URECHOLINE Tablets to 129 postpartum patients reduced the incidence of urinary retention 80 per cent. The dose was 15 to 30 mg. orally, commencing on the patient's return to her room after delivery, and repeated every four to six hours for the first twenty-four hours. This regimen usually eliminates the necessity for exposing the patient to the discomfort and risk of infection inherent in catheterization.

Supplied: 5 mg. and 10 mg. tablets, bottles of 100; 1-cc. ampuls, each containing 5 mg. of URECHOLINE Chloride.

Reference: 1. Fleming, A. R., *Am. J. Obst. & Gynec.*, **64**:134, July 1952.

URECHOLINE IS A TRADEMARK OF MERCK & CO., INC

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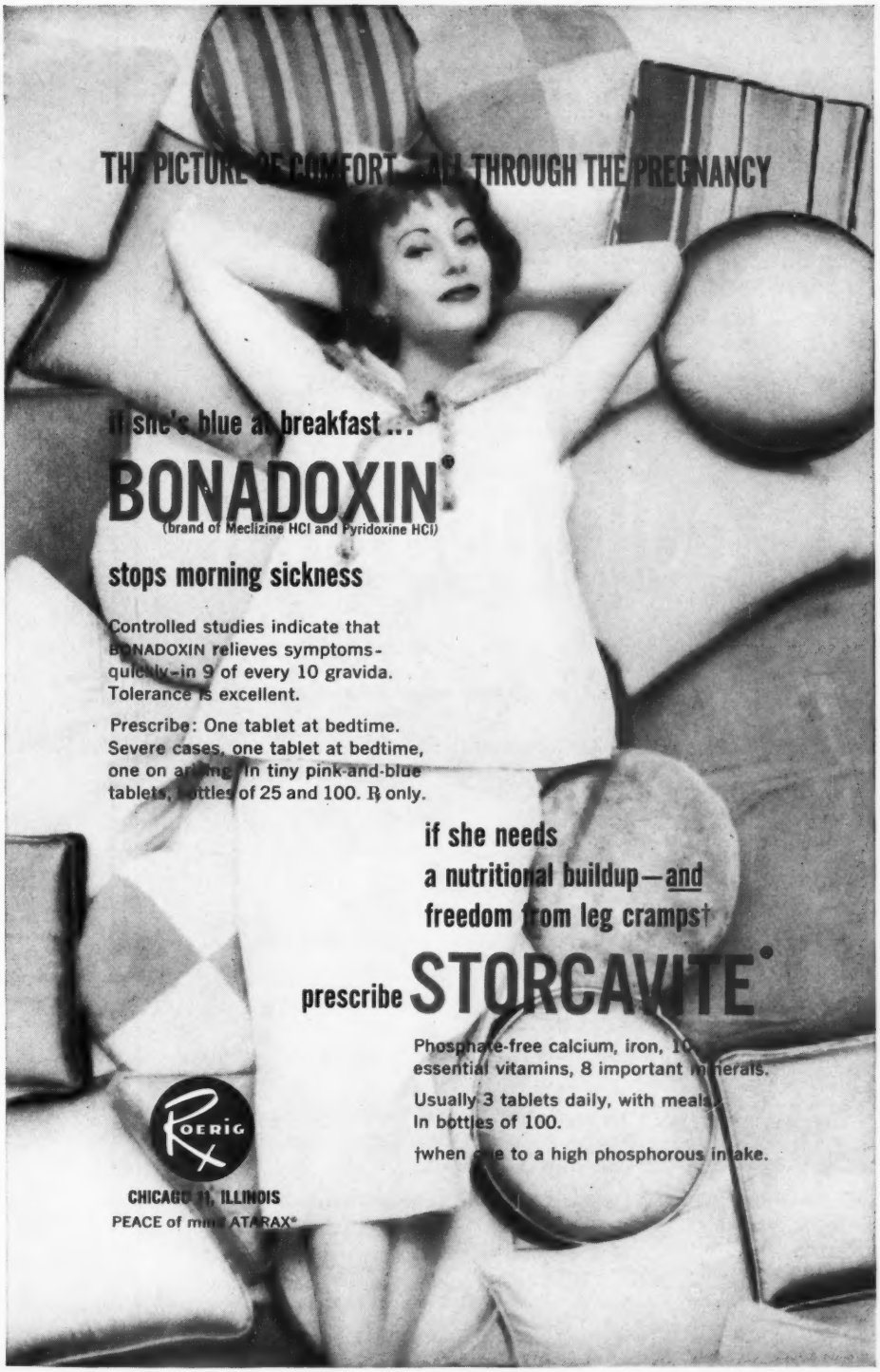
DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.


THE PICTURE OF COMFORT ALL THROUGH THE PREGNANCY
if she's blue at breakfast...
BONADOXIN®
(brand of Meclizine HCl and Pyridoxine HCl)
stops morning sickness
Controlled studies indicate that BONADOXIN relieves symptoms quickly—in 9 of every 10 gravida. Tolerance is excellent.
Prescribe: One tablet at bedtime. Severe cases, one tablet at bedtime, one on arising. In tiny pink-and-blue tablets, bottles of 25 and 100. ℞ only.
if she needs a nutritional buildup—and freedom from leg cramps†
prescribe STORCAVITE®
Phosphate-free calcium, iron, 10 essential vitamins, 8 important minerals.
Usually 3 tablets daily, with meals. In bottles of 100.
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PEACE of mind ATARAX®

for the treatment of

- **AMENORRHEA**
- **FUNCTIONAL UTERINE BLEEDING**
- **HABITUAL ABORTION**
- **LOBULAR HYPERPLASIA**
- **PREMENSTRUAL TENSION**

"colprosterone"®

Vaginal Progesterone

More acceptable
Avoids pain and inconvenience of injection . . . insures better patient cooperation than any other dosage form.

More dependable
Response is more predictable than with oral, or buccal and sublingual therapy.

More economical
Cost is low in terms of greater patient benefits.

"Colprosterone" Vaginal Tablets—Brand of progesterone U.S.P. presented in a specially formulated base to insure maximum absorption and utilization.

Complete dosage regimens for above indications are outlined in descriptive literature. Write for your copy.

Supplied: No. 793—25 mg. tablets (silver foil). No. 794—50 mg. tablets (gold foil). Boxes of 30 and Combination Package of 15 tablets with applicator.

Each tablet is individually and hermetically sealed. Presented in strips of 3 units, detachable as required.

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CLINICAL COLLOQUY

My patients complain that the pain tablets I prescribe are too slow-acting... they usually take about 30 to 40 minutes to work.

Why don't you try the new codeine derivative that's combined with APC for faster, longer-lasting pain relief?

What is it... how fast does it act?

It's Percodan*—relieves pain in *5 to 15 minutes*, with a single dose lasting 6 hours or longer.

How about side effects?

No problem. For example, the incidence of constipation with Percodan* is rare.

Sounds worth trying— what's the average adult dose?

One tablet every 6 hours. That's all.

Where can I get literature on Percodan?

Just ask your Endo detailman or write to:

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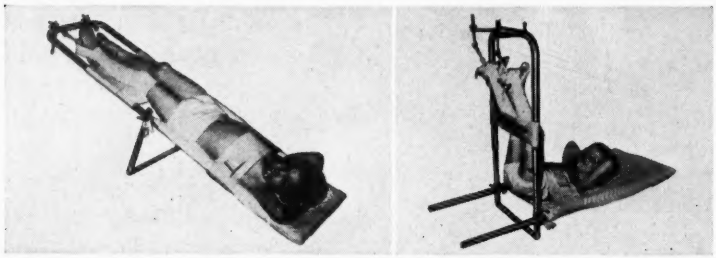
ENDO LABORATORIES

Richmond Hill 18, New York

*U. S. Pat. 2,628,185. PERCODAN contains salts of dihydrohydroxycodeinone and homatropine, plus APC. May be habit-forming. Available through all pharmacies.

THE PORTABLE *Stryker* CHILD'S TRACTION FRAME

for Safe Traction in Children with Fractured Femurs



FOR EXTENSION TRACTION FOR SUSPENSION TRACTION

Actual hospital tests in fractured femur cases of children have shown that the use of the Portable Stryker Child's Traction Frame greatly reduces nursing care. The attending physician can prescribe home convalescence after the first week of the usual six weeks of traction. The frame is ideally suited for children from infancy to ten years of age, easily converts from extension to suspension traction, avoids danger of circulatory complications. Completely portable, sets on any bed, disassembles for storage. Clip coupon for complete information or ordering.

PRICE No. 725 — $58.00

☐ Send me _____ frames. Bill the address below.
☐ Please send me complete details on the Stryker Dual Purpose Child's Traction Frame.

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Hospital: _____

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For
the
patient
adrift
in a
sea
of
troubles...

smooth sailing
with NOLUDAR®

PRODUCT INFORMATION

NOLUDAR 'Roche'

A non-barbiturate sedative-hypnotic

DESCRIPTION: Noludar is a mild sedative-hypnotic with moderately prompt onset and short duration of action. It is <u>not</u> a barbiturate, but a piperidine derivative; chemically, it is 3,3-diethyl-5-methyl-2,4-piperidinedione.

PROPERTIES: Noludar produces refreshing sleep with little likelihood of "hangover" on awakening. Sleep is usually induced within ½ to 1 hour, lasting for 6 to 7 hours. Therapeutic doses of Noludar are, as a rule, well tolerated.

INDICATIONS: Relief of nervous insomnia and daytime tension.

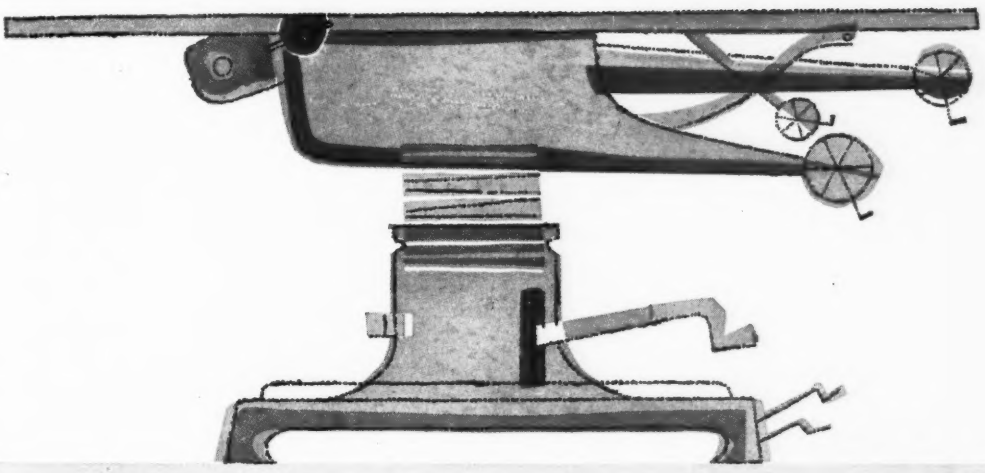
DOSAGE: For nervous insomnia, 200 mg at bedtime; if necessary, another 100 mg may be given after 1½ to 2 hours. For daytime tension, 50 mg three to four times daily.

SUPPLY: Noludar is available in scored tablets of two strengths – 50 mg for sedation and 200 mg for insomnia – and in a palatable, cordial-flavored elixir, 50 mg per teaspoonful (5 cc). Tablets, 50 and 200 mg, bottles of 100; elixir, bottles of 16 oz.

Noludar®-- brand of methyprylon

Hoffmann-La Roche Inc • Nutley 10 • New Jersey

do you have an overweight patient?



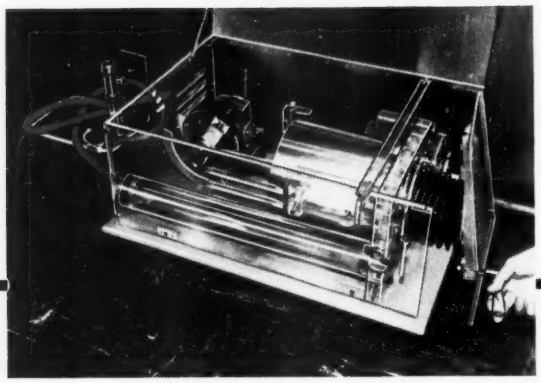
'Dexamyl' (a combination of dextro-amphetamine sulfate, S.K.F., and amobarbital) can smoothly and subtly encourage your patient to hold to the diet you suggest—thereby helping him get ready for surgery. (Furthermore, 'Dexamyl' is useful postoperatively; its mood-ameliorating effect encourages early ambulation.)

DEXAMYL*

tablets • elixir • Spansule† capsules

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off.
†T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.



MÖRCH PISTON RESPIRATOR

For continuous mechanical hyperventilation

(As described in Armamentarium Vol. II—No. VIII)

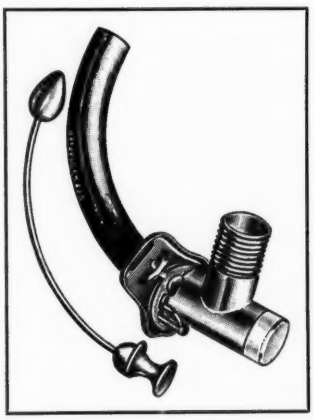
A simple, dependable unit, especially valuable in prevention of paradoxical respiration in crushing injuries of the chest; also in postoperative respiratory insufficiency, poliomyelitis, brain injuries, barbiturate poisoning. Blows humidified air into patient's lungs, with or without added oxygen. Exhalation valve prevents rebreathing. Only two simple adjustments —for rate and volume. Hand bellows for continuous operation in case of power failure or while transporting patient. Compactly assembled in clear plexiglas case.

AS-1665—Each (with two exhalation valves) $1,290.00

MÖRCH SWIVEL TRACHEOSTOMY TUBE

(for use with MÖRCH PISTON RESPIRATOR)

Modified standard Jackson trachea tube with swiveling T-piece for reliable connection between tracheostomy tube and respirator. Prevents inadvertent rotation and twisting of tube . . . does not reduce airway at any point . . . permits easy aspiration of secretions. May be boiled or autoclaved. Tube Size 4. (BE-214) and Tube Size 6 (BE-216) Each $20.50; Tube Size 8 (BE-218) Each $22.50.



Armamentarium

MUELLER & CO.

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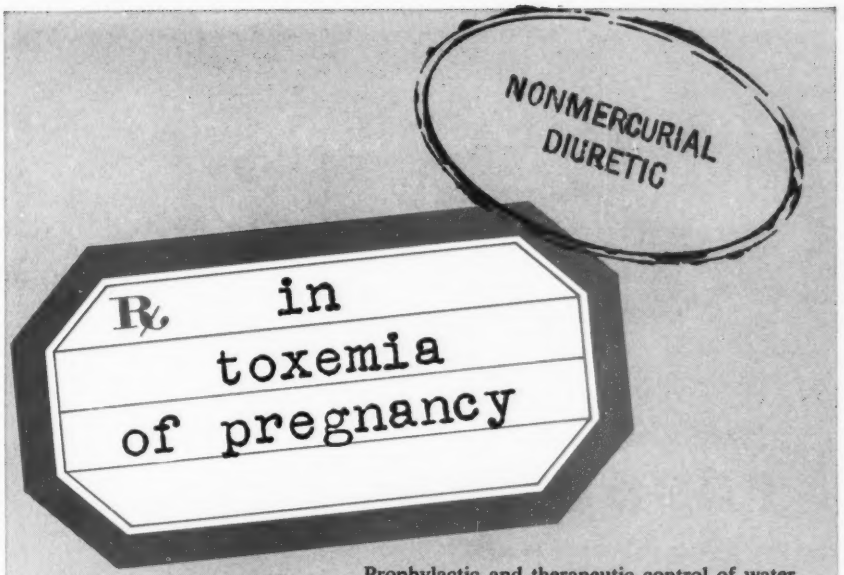

Prophylactic and therapeutic control of water retention in toxemia of pregnancy may be effectively maintained by DIAMOX.

DIAMOX is a highly versatile diuretic, effective in the *mobilization of edema fluid* and in the *prevention of fluid accumulation*—with transient, readily reversible, blood electrolyte changes.

Well-tolerated orally, a single dose is active for 6 to 12 hours, offering convenient *daytime diuresis* and *nighttime rest.*

DIAMOX is of proven value in other conditions as well, including cardiac edema, acute glaucoma, epilepsy, premenstrual tension.

Ease of administration, low toxicity, lack of renal and gastrointestinal irritation make its use simple and singularly free of complications.

Supplied: scored tablets of 250 mg. (Also in ampuls of 500 mg. for parenteral use).

Diamox*

ACETAZOLAMIDE LEDERLE

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AMERICAN CYANAMID COMPANY
PEARL RIVER, NEW YORK

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OHIO

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guaranteed

STRENGTH

when strength counts

TENSO-*Pli* sutures exceed U.S.P. strength requirements by 50% or more. Every lot of size 2/0 material passes the U.S.P. test for size 0. Every lot of size 0 passes the test for size 1. This is not accidental, but the result of rigid testing. We are so sure of your satisfaction that *we have printed a written guarantee on each label,* together with the knot strength of each lot. When extra strength is a necessity, be sure . . . specify TENSO-*Pli.*

TENSO-*Pli* is the only surgical suture with individually formulated solutions for each size. This assures maximum pliability, resistance to fraying, and controlled absorption.

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in postmenopausal vaginitis
in vaginal plastic surgery

ORTHO®

Dienestrol CREAM

vaginal estrogen therapy

builds vaginal epithelium

CONCLUSIONS:

after 2 years of extensive clinical use of...

RECTAL DESITIN® OINTMENT

"it has fulfilled better than any previously tried medicaments all the qualifications" expected of a proctologic ointment[1]

"promotes smooth epithelization and healthy granulation tissue and accelerates healing."[1]

- Specially formulated for prolonged, unusual efficacy in relieving pain, itching, irritation and inflammation in non-surgical HEMORRHOIDS, PRURITUS ANI, FISSURES, PERIANAL DERMATITIS, PAPILLITIS, etc. Non-sensitizing.

Formula: **RECTAL** DESITIN OINTMENT contains high grade Norwegian cod liver oil, zinc oxide, lanolin, talcum, sodium lauryl sulfate, petrolatum q.s. Does **not** contain local anesthetics, narcotics, or "caine" drugs which might mask serious anorectal disorders.

Available on your prescription in tubes of 1½ oz., with a safe, flexible applicator

Liberal SAMPLE supply on request

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New **RECTAL** DESITIN OINTMENT is not to be confused with regular DESITIN OINTMENT

1. Spiesman, M. G. and Malow, L.: Amer. J. Proctology, June 1956.

relaxes both mind and muscle

for anxiety and tension in everyday practice

- well suited for prolonged therapy
- well tolerated, relatively nontoxic
- no blood dyscrasias, liver toxicity, Parkinson-like syndrome or nasal stuffiness
- chemically unrelated to phenothiazine compounds and rauwolfia derivatives
- orally effective within 30 minutes for a period of 6 hours

For treatment of **anxiety and tension states and muscle spasm**

THE ORIGINAL MEPROBAMATE

Miltown®

2-methyl-2-n-propyl-1,3-propanediol dicarbamate—U. S. Patent 2,724,720

Tranquilizer with muscle-relaxant action

NOW IN 2 CONVENIENT DOSAGES

NEW 200 mg. SUGAR-COATED TABLETS

STANDARD 400 mg. SCORED TABLETS

DISCOVERED AND INTRODUCED BY WALLACE LABORATORIES, *New Brunswick, N. J.*

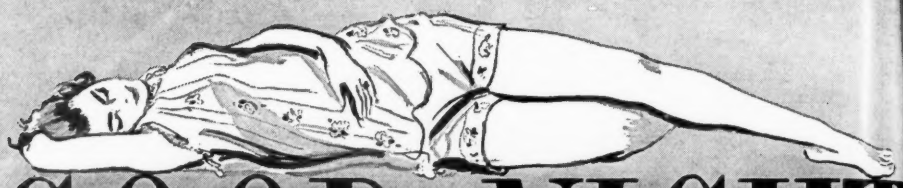
THE MILTOWN® MEPROBAMATE MOLECULE

SUPPLIED : *400 mg. scored tablets*
200 mg. sugar-coated tablets

USUAL DOSAGE : *One or two 400 mg. tablets t.i.d.*

Literature and Samples Available on Request

CH-3707-BS



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PATIENTS SLEEP SOUNDLY with non-barbiturate Doriden—0.5 Gm. at bedtime. Onset of action is smooth and gradual (without preliminary excitation). Effect lasts 4 to 8 hours.

Doriden®

(glutethimide CIBA)

SUPPLY: Tablets, 0.125 Gm. (white), 0.25 Gm. (white, scored), and 0.5 Gm. (white, scored).

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PATIENTS AWAKE ALERT AND REFRESHED; Doriden is rapidly metabolized, allows restful natural slumber without hangover.

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